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<b>(21) International Application Number:</b> PCT/JP99/03929 <b>(22) International Filing Date:</b> 22 July 1999 (22.07.1999) <b>(30) Priority Data:</b> 10/208820 24 July 1998 (24.07.1998) JP 10/224105 07 August 1998 (07.08.1998) JP 10/238116 25 August 1998 (25.08.1998) JP 10/254736 09 September 1998 (09.09.1998) JP 10/275505 29 September 1998 (29.09.1998) JP <b>(60) Parent Application or Grant</b> SAGAMI CHEMICAL RESEARCH CENTER [/]; ( ). PROTEGENE INC. [/]; ( ). KATO, Seishi [/]; ( ). KIMURA, Tomoko [/]; ( ). KATO, Seishi [/]; ( ). KIMURA, Tomoko [/]; ( ). AOYAMA, Tamotsu : ( ).	<b>Published</b>
<b>(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS</b> <b>(54) Titre: PROTEINES HUMAINES A DOMAINES HYDROPHOBES ET ADN CODANT POUR CES PROTEINES</b>  <b>(57) Abstract</b> <p>The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.</p> <b>(57) Abrégé</b> <p>L'invention concerne des protéines humaines à domaines hydrophobes, des ADN codant pour ces protéines, et des vecteurs d'expression pour ces ADN, ainsi que des cellules eucaryotes exprimant ces ADN.</p>	

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(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS			
(57) Abstract  The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.			

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## Description

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## DESCRIPTION

Human Proteins Having Hydrophobic  
Domains and DNAs Encoding These Proteins

TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies against these proteins. The human cDNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be utilized as gene sources for large-scale production of the proteins encoded by these cDNAs. Cells into which these genes are introduced to express secretory proteins and membrane proteins in large amounts can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

BACKGROUND ART

Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal manner such as the injection or the drip, so that there are

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hidden potentialities as medicines. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents, etc. have been currently employed as medicines. In addition, secretory proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Because it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes coding for them is expected to lead to development of novel pharmaceuticals utilizing these proteins.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters, etc. in the material transportation and the information transmission through the cell membrane. Examples thereof include receptors for a variety of cytokines, ion channels for the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on, where the genes for many of them have been cloned already. It has been clarified that abnormalities of these membrane proteins are associated with a number of hitherto-cryptogenic diseases. Therefore, discovery of a new membrane protein is anticipated to lead to elucidation of the causes of many diseases, so that isolation of a new gene coding for the membrane protein has been desired.

Heretofore, owing to difficulty in the purification from human cells, these secretory proteins and membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises introduction of a cDNA library into eucaryotic cells to express cDNAs and then screening of the cells secreting, or expressing on the surface of membrane,

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the objective active protein. However, this method is applicable only to cloning of a gene for a protein with a known function.

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In general, secretory proteins and membrane proteins possess at least one hydrophobic domain inside the proteins, wherein, after synthesis thereof in the ribosome, this domain works as a secretory signal or remains in the phospholipid membrane to be trapped in the membrane. Accordingly, the evidence of this cDNA for encoding a secretory protein and a membrane protein is provided by determination of the whole base sequence of a full-length cDNA followed by detection of highly hydrophobic domain(s) in the amino acid sequence of the protein encoded by this cDNA.

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#### OBJECTS OF THE INVENTION

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The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as transformed eucaryotic cells that are capable of expressing these DNAs. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

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#### BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01550.

Fig. 2 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02593.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10195.

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Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10423.

Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10506.

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5 Fig. 6 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10507.

Fig. 7 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10548.

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10 Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10566.

Fig. 9 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10567.

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Fig. 10 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10568.

16 Fig. 11 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01426.

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Fig. 12 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02515.

Fig. 13 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02575.

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20 Fig. 14 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10357.

Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10447.

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26 Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10477.

Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10513.

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Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10540.

30 Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10557.

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Fig. 20 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10563.

Fig. 21 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01467.

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Fig. 22 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01956.

Fig. 23 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02545.

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Fig. 24 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02551.

Fig. 25 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

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Fig. 26 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02632.

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Fig. 27 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10488.

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Fig. 28 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10538.

Fig. 29 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10542.

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Fig. 30 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10571.

Fig. 31 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01470.

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Fig. 32 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02419.

Fig. 33 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

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Fig. 34 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02695.

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Fig. 35 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10031.

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Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10530.

Fig. 37 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10541.

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Fig. 38 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10550.

Fig. 39 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10590.

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Fig. 40 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10591.

Fig. 41 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01462.

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Fig. 42 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02485.

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Fig. 43 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02798.

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Fig. 44 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10041.

Fig. 45 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10246.

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Fig. 46 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10392.

Fig. 47 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10489.

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Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10519.

Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10531.

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Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10574.

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#### SUMMARY OF THE INVENTION

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As the result of intensive studies, the present inventors have been successful in cloning of cDNAs coding for proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention. In other words, the present invention provides human proteins having hydrophobic domains, namely proteins comprising any of the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. Moreover, the present invention provides DNAs coding for the above-mentioned proteins, exemplified by cDNAs comprising any of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140, as well as expression vectors that are capable of expressing any of these DNAs by in vitro translation or in eucaryotic cells and transformed eucaryotic cells that are capable of expressing these DNAs and of producing the above-mentioned proteins.

#### DETAILED DESCRIPTION OF THE INVENTION

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The proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc., a method for preparation of peptides by the chemical synthesis, or a method for production with the recombinant DNA technology using the DNAs coding for the hydrophobic domains of the present invention, among which the method for production with the recombinant DNA technology is employed preferably. For instance, in vitro expression of the proteins can be achieved by preparation of an RNA by in vitro transcription from a vector having one of the cDNAs of the present invention, followed by in vitro translation using this RNA as a template. Also, introduction of the translated region into a suitable expression vector

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by the method known in the art leads to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eucaryotic cells such as yeasts, insect cells, mammalian cells, etc.

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5 In the case where one of the proteins of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro, when the translated region of this cDNA is introduced into a vector having an RNA polymerase promoter, followed by addition of the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, containing an RNA polymerase corresponding to the promoter. RNA polymerase promoters are exemplified by T7, T3, SP6, and the like. The vectors containing these RNA polymerase promoters are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II, and so on. Furthermore, the protein of the present invention can be expressed as the secreted form or the form incorporated into the microsome membrane, when a canine pancreas microsome or the like is added to the reaction system.

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25 In the case where one of the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli* etc., a recombinant expression vector bearing the translated region of the cDNA of the present invention is constructed in an expression vector having an origin which can be replicated in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator etc. and, after transformation of the host cells with this expression vector, the resulting transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the

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microorganism. In this case, a protein fragment containing any region can be obtained by carrying out the expression with inserting an initiation codon and a termination codon in front of and behind the selected translated region. Alternatively, a fusion protein with another protein can be expressed. Only the portion of the protein encoded by this cDNA can be obtained by cleavage of this fusion protein with a suitable protease. The expression vector for *Escherichia coli* is exemplified by the pUC series, pBluescript II, the pET expression system, the pGEX expression system, and so on.

In the case where one of the proteins of the present invention is produced by expressing the DNA in eucaryotic cells, the protein of the present invention can be produced as a secretory protein or as a membrane protein on the cell-membrane surface, when the translated region of this cDNA is introduced into an expression vector for eucaryotic cells that has a promoter, a splicing region, a poly(A) addition site, etc., followed by introduction into the eucaryotic cells. The expression vector is exemplified by pKAl, pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, and so on. Examples of eucaryotic cells to be used in general include mammalian cultured cells such as simian kidney cells COS7, Chinese hamster ovary cells CHO, etc., budding yeasts, fission yeasts, silkworm cells, *Xenopus* oocytes, and so on, but any eucaryotic cells may be used, provided that they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eucaryotic cells by methods known in the art such as the electroporation method, the calcium phosphate method, the liposome method, the DEAE-dextran method, and so on.

After one of the proteins of the present invention is

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expressed in prokaryotic cells or eucaryotic cells, the objective protein can be isolated from the culture and purified by a combination of separation procedures known in the art. Such examples include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic chromatography, affinity chromatography, reverse phase chromatography, and so on.

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The proteins of the present invention include peptide fragments (5 amino acid residues or more) containing any partial amino acid sequence in the amino acid sequences represented by SEQ ID Nos. 1. to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Hereupon, among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins, after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP 8-187100 A]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secretory forms. Such proteins or peptides in the secretory forms shall come within the scope of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences, expression in appropriate eucaryotic cells affords proteins to which sugar chains are attached. Accordingly, such proteins or peptides to which sugar chains are attached shall come within the

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scope of the present invention.

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The DNAs of the present invention include all the DNAs coding for the above-mentioned proteins. These DNAs can be obtained by using a method by chemical synthesis, a method by cDNA cloning, and so on.

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The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. These cDNAs are synthesized by using as templates poly(A)<sup>+</sup> RNAs extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available, human cDNA libraries can be utilized. Cloning of the cDNAs of the present invention from the cDNA libraries can be carried out by synthesis of an oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention, followed by screening using this oligonucleotide as the probe according to the colony or plaque hybridization by a method known in the art. In addition, the cDNA fragments of the present invention can be prepared by synthesis of oligonucleotides which hybridize with both termini of the objective cDNA fragment, followed by the usage of these oligonucleotides as the primers for the RT-PCR method using an mRNA isolated from human cells.

The cDNAs of the present invention are characterized by

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comprising either of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA was obtained, the total base number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.



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Table 1

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SEQ ID No.	HP number	Cells	Base number	Number of amino acid residues
1, 11, 21	HP01550	Stomach cancer	510	125
2, 12, 22	HP02593	Saos-2	697	131
3, 13, 23	HP10195	HT-1080	1619	242
4, 14, 24	HP10423	U-2 OS	1066	264
5, 15, 25	HP10506	Stomach cancer	618	112
6, 16, 26	HP10507	Stomach cancer	1021	146
7, 17, 27	HP10548	Stomach cancer	1432	344
8, 18, 28	HP10566	Stomach cancer	601	97
9, 19, 29	HP10567	Stomach cancer	585	124
10, 20, 30	HP10568	Stomach cancer	1100	327
31, 41, 51	HP01426	Stomach cancer	1065	313
32, 42, 52	HP02515	Saos-2	937	229
33, 43, 53	HP02575	Saos-2	1678	467
34, 44, 54	HP10357	Stomach cancer	467	99
35, 45, 55	HP10447	Liver	875	189
36, 46, 56	HP10477	Liver	1256	363
37, 47, 57	HP10513	Stomach cancer	884	249
38, 48, 58	HP10540	Saos-2	589	98
39, 49, 59	HP10557	Stomach cancer	673	172
40, 50, 60	HP10563	Saos-2	1425	120
61, 71, 81	HP01467	HT-1080	1436	307
62, 72, 82	HP01956	Liver	997	183
63, 73, 83	HP02545	Saos-2	1753	327
64, 74, 84	HP02551	Saos-2	1117	223
65, 75, 85	HP02631	Saos-2	1380	48
66, 76, 86	HP02632	HT-1080	1503	371
67, 77, 87	HP10488	Liver	733	90
68, 78, 88	HP10538	Saos-2	3768	499
69, 79, 89	HP10542	Stomach cancer	770	106
70, 80, 90	HP10571	Stomach cancer	1229	152

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91, 101, 111	HP01470	Stomach cancer	1619	358
92, 102, 112	HP02419	Stomach cancer	2054	226
93, 103, 113	HP02631	Saos-2	1380	195
94, 104, 114	HP02695	Stomach cancer	1292	339
95, 105, 115	HP10031	Saos-2	2168	487
96, 106, 116	HP10530	Saos-2	1357	393
97, 107, 117	HP10541	Stomach cancer	711	196
98, 108, 118	HP10550	Stomach cancer	651	107
99, 109, 119	HP10590	HT-1080	1310	350
100, 110, 120	HP10591	HT-1080	1400	107
121, 131, 141	HP01462	HT-1080	2050	483
122, 132, 142	HP02485	Stomach cancer	2746	334
123, 133, 143	HP02799	HT-1080	1136	267
124, 134, 144	HP10041	Saos-2	619	106
125, 135, 145	HP10246	KB	864	224
126, 136, 146	HP10392	U-2 OS	1527	258
127, 137, 147	HP10489	Stomach cancer	659	110
128, 138, 148	HP10519	Stomach cancer	710	91
129, 139, 149	HP10531	Saos-2	2182	344
130, 140, 150	HP10574	Stomach cancer	2773	428

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Hereupon, the same clones as the cDNAs of the present invention can be easily obtained by screening of the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention by the use of an oligonucleotide probe synthesized on the basis of the cDNA base sequence described in any of SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and 131 to 150.

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In general, the polymorphism due to the individual difference is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are inserted, deleted and/or substituted with other nucleotides in SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and

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131 to 150 shall come within the scope of the present invention.

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In a similar manner, any protein in which one or plural amino acids are inserted, deleted and/or substituted with other amino acids shall come within the scope of the present invention, as far as the protein possesses the activity of any protein having the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

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The cDNAs of the present invention include cDNA fragments (10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or in the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

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In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

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#### Research Uses and Utilities

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The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

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protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine

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levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be

administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular

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Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

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5 Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and  
10 Measurement of mouse and human Interferon  $\gamma$ , Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

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Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without  
15 limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-  
20 1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6-  
35 Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 -  
40 Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991;  
45 Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.  
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6.13.1, John Wiley and Sons, Toronto. 1991.

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Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp.



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and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

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Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

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Using the proteins of the invention it may also be possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent

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has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

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5 Down regulating or preventing one or more antigen  
functions (including without limitation B lymphocyte antigen  
functions (such as , for example, B7)), e.g., preventing  
high level lymphokine synthesis by activated T cells, will  
be useful in situations of tissue, skin and organ  
transplantation and in graft-versus-host disease (GVHD).  
10 For example, blockage of T cell function should result in  
reduced tissue destruction in tissue transplantation.  
Typically, in tissue transplants, rejection of the  
transplant is initiated through its recognition as foreign  
by T cells, followed by an immune reaction that destroys the  
15 transplant. The administration of a molecule which inhibits  
or blocks interaction of a B7 lymphocyte antigen with its  
natural ligand(s) on immune cells (such as a soluble,  
monomeric form of a peptide having B7-2 activity alone or in  
conjunction with a monomeric form of a peptide having an  
20 activity of another B lymphocyte antigen (e.g., B7-1, B7-3)  
or blocking antibody), prior to transplantation can lead to  
the binding of the molecule to the natural ligand(s) on the  
immune cells without transmitting the corresponding  
costimulatory signal. Blocking B lymphocyte antigen  
25 function in this matter prevents cytokine synthesis by  
immune cells, such as T cells, and thus acts as an  
immunosuppressant. Moreover, the lack of costimulation may  
also be sufficient to anergize the T cells, thereby inducing  
tolerance in a subject. Induction of long-term tolerance by  
30 B lymphocyte antigen-blocking reagents may avoid the  
necessity of repeated administration of these blocking  
reagents. To achieve sufficient immunosuppression or

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tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

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The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

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Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating

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autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the commoncold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the

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transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

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In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

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The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain protein and , microglobulin protein or an MHC class

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II chain protein and an MHC class II chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

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The activity of a protein of the invention may, among other means, be measured by the following methods:

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Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J.

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Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

5 Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

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Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

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Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965,

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1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

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5 Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

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Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

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#### Hematopoiesis Regulating Activity

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A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to

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stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and

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Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

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Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

#### Tissue Growth Activity

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A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

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A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is

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not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

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in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head

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trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

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Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

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It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

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A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

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A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

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The activity of a protein of the invention may, among other means, be measured by the following methods:

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Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);

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International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

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5 Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

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Activin/Inhibin Activity

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A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among

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other means, be measured by the following methods:

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Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

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10 A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

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25 A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

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The activity of a protein of the invention may, among

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other means, be measured by the following methods:

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Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

#### Hemostatic and Thrombolytic Activity

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A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

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The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include,

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without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

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#### Receptor/Ligand Activity

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A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

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The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22),

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Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987;  
Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein  
et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et  
al., J. Immunol. Methods 175:59-68, 1994; Stitt et al.,  
Cell 80:661-670, 1995.

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#### Anti-Inflammatory Activity

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Proteins of the present invention may also exhibit  
anti-inflammatory activity. The anti-inflammatory activity  
may be achieved by providing a stimulus to cells involved in  
the inflammatory response, by inhibiting or promoting cell-  
cell interactions (such as, for example, cell adhesion), by  
inhibiting or promoting chemotaxis of cells involved in the  
inflammatory process, inhibiting or promoting cell  
extravasation, or by stimulating or suppressing production  
of other factors which more directly inhibit or promote an  
inflammatory response. Proteins exhibiting such activities  
can be used to treat inflammatory conditions including  
chronic or acute conditions), including without limitation  
inflammation associated with infection (such as septic shock,  
sepsis or systemic inflammatory response syndrome (SIRS)),  
ischemia-reperfusion injury, endotoxin lethality, arthritis,  
complement-mediated hyperacute rejection, nephritis,  
cytokine or chemokine-induced lung injury, inflammatory  
bowel disease, Crohn's disease or resulting from over  
production of cytokines such as TNF or IL-1. Proteins of the  
invention may also be useful to treat anaphylaxis and  
hypersensitivity to an antigenic substance or material.

#### Tumor Inhibition Activity

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In addition to the activities described above for  
immunological treatment or prevention of tumors, a protein  
of the invention may exhibit other anti-tumor activities. A

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Other Activities

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protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of

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embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

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#### Examples

The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic operations with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the manufacturer's instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

#### (1) Selection of cDNAs Encoding Proteins Having Hydrophobic Domains

The cDNA library of fibrosarcoma cell line HT-1080 (WO98/11217), the cDNA library of osteosarcoma cell line Saos-2 (WO97/33993), the cDNA library of osteosarcoma cell line U-2 OS (WO98/21328), the cDNA library of epidermoid

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carcinoma cell line KB (WO98/11217), the cDNA library of tissues of stomach cancer delivered by the operation (WO98/21328), the cDNA library of liver tissue delivered by the operation (WO98/21328), and were used for the cDNA libraries. Full-length cDNA clones were selected from respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. Any clone that has a hydrophobic region being putative as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

#### (2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present invention was used for in vitro transcription/translation with a T<sub>7</sub>T rabbit reticulocyte lysate kit (Promega). In this case, [<sup>35</sup>S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit. Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25  $\mu$ l containing 12.5  $\mu$ l  $\mu$  of T<sub>7</sub>T rabbit reticulocyte lysate, 0.5  $\mu$ l of a buffer solution (attached to the kit), 2  $\mu$ l of an amino acid mixture (without methionine), 2  $\mu$ l of [<sup>35</sup>S]methionine (Amersham) (0.37 MBq/ $\mu$ l), 0.5  $\mu$ l of T7 RNA polymerase, and 20 U of RNasin. Also, an experiment in the presence of a membrane system was carried

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out by adding to this reaction system 2.5  $\mu$ l of a canine pancreas microsomal fraction (Promega). To 3  $\mu$ l of the resulting reaction solution was added 2  $\mu$ l of the SDS sampling buffer (125 mM Tris-hydrochloric acid buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography.

(3) Expression by COS7

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*Escherichia coli* cells bearing the expression vector for the protein of the present invention was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100  $\mu$ g/ml of ampicillin, the helper phage M13K07 (50  $\mu$ l) was added, and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100  $\mu$ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

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The cultured cells derived from simian kidney, COS7, were incubated at 37°C in the presence of 5% CO<sub>2</sub> in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf serum. Into a 6-well plate (Nunc, well diameter: 3 cm) were inoculated with  $1 \times 10^5$  COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO<sub>2</sub>. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the resulting cells was added a suspension of 1  $\mu$ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3  $\mu$ l of

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TRANSFECTAM™ (IBF) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO<sub>2</sub>. After the sample solution was removed, the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO<sub>2</sub>. After the culture medium was replaced by a culture medium containing [<sup>35</sup>S]cystine or [<sup>35</sup>S]methionine, the incubation was carried out for one hour. After the culture medium and the cells were separated by centrifugation, proteins in the culture medium fraction and the cell-membrane fraction were subjected to SDS-PAGE.

(4) Clone Examples

<HP01550> (SEQ ID Nos. 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP01550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 65-bp 5'-untranslated region, a 378-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 125 amino acid residues and there existed one putative transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 15 kDa that was almost identical with the molecular weight of 13,825 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein F45G2.c (GenBank Accession No. Z93382). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C.

*C. elegans* hypothetical protein F45G2.c (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.5% in the entire region.

Table 2

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10 HP MAKYLAQIIIVMGVVGRAFARALRQEF-----AASRAAADARGRAGHRSAAASNLS-
      . . . . * . * . * . * . * .   ** . ** . . . . * . * . **
CE MPWRTALKVALAAGEAVAKALTRAVRDEIKQTQQAAARHAASTGQSASETRENANSNAKL
HP GLSLQEAAQIILNV-SKLSPEEVQKNYEHLFKVNDKSVGGSFYLQSKVVRAKERLDEEL-K
    * . * . * . ***** . * . ***** . ***** . ***** ***** . *** .
15 CE GISLEESQLIILNVTPLNREEVEKHIEHLFNINDKSKGGTLYLQSKVFRAKERIDEEFGFGR
HP IQAQEDREKGMPHT
    * . * . * . . . *
CE IELKEEKKKEENAKTE
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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA338859) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02593> (SEQ ID Nos. 2, 12, and 22)

Determination of the whole base sequence of the cDNA insert of clone HP02593 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 103-bp 5'-untranslated region, a 396-bp ORF,



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and a 198-bp 3'-untranslated region. The ORF codes for a protein consisting of 131 amino acid residues and there existed four putative transmembrane domains at the C-terminus. Figure 2 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to a human OB-R gene-related protein (EMBL Accession No. Y12670). Table 3 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human OB-R gene-related protein (OB). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the entire region.

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Table 3

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HP MAGIKALISLSFGGAIGLMLGLGALPIYNKYWPLFVLFPYILSPIPYCIARRLVDDTD  
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 OB MAGVKALVALSFGGAIGLTFMLGLGALEDYGVYWPLFVLIFHAISPIPHFIAKRVTYDSD  
 HP AMSNACKELAIPLTTGIVVSAPGLPIVFARAHLEWGACALVLTGNTVIFATILGFPLVF  
 \*\*,\*\*\*,\*\*\*,\*\*\*\*\* \*\*\*\*\*\*,\*\*\*,\*\*\*,\*\*\*\*\* \*\*\*\*\*\*,\*\*\*,\*\*\*,\*\*  
 OB ATSSACRELAYFFTTGIVVSAPGFPPVILARVAVIKWGACGLVLGNAVIFLTIQGFPLIF  
 HP GSNDDFSQQQW  
 \*,\*\*\*\*\*,\*\*  
 OB GRGDDFSWEQW

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA306490) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10195> (SEQ ID Nos. 3, 13, and 23)

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Determination of the whole base sequence of the cDNA insert of clone HP10195 obtained from cDNA library of human fibrosarcoma HT-1080 revealed the structure consisting of a 286-bp 5'-untranslated region, a 729-bp ORF, and a 604-bp 3'-untranslated region. The ORF codes for a protein consisting of 242 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was somewhat larger than the molecular weight of 27,300 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the supernatant fraction and the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein has revealed the registration of sequences that were similar to the Aplysia VAP-33 (SWISS-PROT Accession No. P53173). Table 4 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the Aplysia VAP-33 (AP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the

present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 46.5% in the entire region.

Table 4

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HP MAKHEQILVLOPPTDLKPKGFPTDVVTNLKLRNPSDRKVCFKVKTAPRRYCVRPNSGI
  *.*** *.***.***.***.***.***.***.***.***.***.***.***.***.***
AP MASHEQALILEPAGELRFKGFPTDVVTADLKLNSPTDRRICFKVKTAPKRYCVRPNSGI
HP IDPGSTVTVSVMLQFFDYDPNEKSKHKFMVQTIFFAPPNTSD-MEAVWKEAKPDELMDSKL
  ..* .....***.***.***.***.***.***.***.***.***.***.***.***
AP LEPKTSIAVAVMLQFFNYDPNEKNKHKFMVQSMYAPDHVVESQELLWKDAPPESLMDTKL
HP RCVFEMPENNDKLNDEPSK-----AVPLNASKQDGPMPKP-HSVSLNDTE
  *****.....*.***.***.***.***.***.***.***.***.***.***.***
AP RCVFEMPDGSHQAPASDASRATDAGAHFSZSALEDPTVASRKTETQSPKRVGAVGSAGED
HP TRKLMECKRLQGEMMKLSEENRHLRDEGLRLRKVAHSD--KPGSTSTASFRDNVTSPLP
  ..**.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*
AP VKKLQHELKKAQSEITSLKGENSEQLKDEGIRLRKVAMTDTVSPTPLNPSAPAAAVRAFP
HP SLLVVIAAIPIGFPLGKPIIL
  ...*.***.***.***.***.***.***.***.***.***.***.***.***
AP PVVYVVAAILGLIIGKPLL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA447905) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10423> (SEQ ID Nos. 4, 14, and 24)

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Determination of the whole base sequence of the cDNA insert of clone HP10423 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure consisting of a 64-bp 5'-untranslated region, a 795-bp ORF, and a 207-bp 3'-untranslated region. The ORF codes for a protein consisting of 264 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was almost identical with the molecular weight of 29,377 predicted from the ORF. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D80116) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10506> (SEQ ID Nos. 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10506 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 53-bp 5'-untranslated region, a 339-bp ORF, and a 226-bp 3'-untranslated region. The ORF codes for a protein consisting of 112 amino acid residues and there existed one putative transmembrane domain. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

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Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,821 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282544) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10507> (SEQ ID Nos. 6, 16, and 26)

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Determination of the whole base sequence of the cDNA insert of clone HP10507 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 412-bp 5'-untranslated region, a 441-bp ORF, and a 168-bp 3'-untranslated region. The ORF codes for a protein consisting of 146 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 16,347 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they

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are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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5 <HP10548> (SEQ ID Nos. 7, 17, and 27)

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Determination of the whole base sequence of the cDNA insert of clone HP10548 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 330-bp 5'-untranslated region, a 1035-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed four putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA143152) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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25 <HP10566> (SEQ ID Nos. 8, 18, and 28)

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Determination of the whole base sequence of the cDNA insert of clone HP10566 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 61-bp 5'-untranslated region, a 294-bp ORF, and a 246-bp 3'-untranslated region. The ORF codes for a protein consisting of 97 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 8 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,452 predicted from the ORF. When expressed in COS7 cells, an expression product of about 12 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W79821) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10567> (SEQ ID Nos. 9, 19, and 29)

Determination of the whole base sequence of the cDNA insert of clone HP10567 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 77-bp 5'-untranslated region, a 375-bp ORF, and a 133-bp 3'-untranslated region. The ORF codes for a protein consisting of 124 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 14,484 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA428475) in ESTs, but, since they

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are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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5 <HP10568> (SEQ ID Nos. 10, 20, and 30)

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Determination of the whole base sequence of the cDNA insert of clone HP10568 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 56-bp 5'-untranslated region, a 984-bp ORF, and a 60-bp 3'-untranslated region. The ORF codes for a protein consisting of 327 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36.5 kDa that was almost identical with the molecular weight of 34,326 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Leu-Thr at position 138 and Asn-Leu-Ser at position 206). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from valine at position 24. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein has revealed that the protein was similar to the human cell-surface A33 antigen



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(SWISS-PROT Accession No. Q99795). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human cell-surface A33 antigen (A3). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.0% in the N-terminal region of 243 residues.

Table 5

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HP	MAELPGPFLLCGALLGFLCLSGLA	VEVKVPTEPLSTPLGKTAELTCTYSTSV	GDSPAL-EW
		*.....*	.....*
A3	MVGKMWPVLWTLCAVRVTVD	DAISVETPQDVL	RASQGKSVTLPC
HP	SFVQPGKPISESHPI	LYFTNGHLYPTGSKSKRV	SLQNPP
	..	..*	..*
A3	DKLL--LTH	TERVVVVPF	SNKN-YIH
HP	LCQVNNPPDFY	TNGLGLINLTVLV	PPSNPLCSQSGQT
	* ..	..*	..*
A3	ECSVSLMSD	LEGNTKSRVRL	LVLP
HP	VR	LGTFPTSPGSMVQ	DEVSGQLILTNLSLT
	* ..	..*	..*
A3	KRYN	ILNQEQP--LAQ	PASGQPVSLKNIST
HP	-QGRVAGALIGVLL	GVLLLSVA	AFCLVRFQKERGKPKETY
	..*	..*	..*
A3	NVALYV	GI	AVGVVAALIIIGII
HP	MRADSSKGF	LERPSSASTV	TTT
A3	EREEEDDYRQ	EEQRSTGR	ESPDHLDQ

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

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of sequences that shared a homology of 90% or more (for example, Accession No. T24595) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP01426> (SEQ ID Nos. 31, 41, and 51)

Determination of the whole base sequence of the cDNA insert of clone HP01426 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 1-bp 5'-untranslated region, a 942-bp ORF, and a 122-bp 3'-untranslated region. The ORF codes for a protein consisting of 313 amino acid residues and there existed a putative secretory signal. Figure 11 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 34,955 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 38 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ser-Ser at position 163). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from tryptophan at position 17. When expressed in COS7 cells, an expression product of about 39 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the

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protein was similar to the *Xenopus laevis* cortical granule lectin (EMBL Accession No. X82626). Table 6 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *X. laevis* cortical granule lectin (XL). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the region other than the N-terminal region.

Table 6

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HP MNQLSFLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIRDECPSAFDGLYFLRT
  *   **               *           ***** . * * * * *
XL MLVHILLLLVTGGLSQSCEPVVIVASKNMVKQLDCDKFRSCKEIKDSNEEAQDGIITLTS
HP ENGVIIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANY
  .. . ***** . ***** * * * * * . *****
XL SDGISYQTFCDMTTNGGGWTLVASVHENNMAGKCTIGDRWSSQQGNRADYPEGDGNWANY
HP NTFGSAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLG
  ***** . ***** * * * * * . ***** * * * * *
XL NTFGSAGGATSDDYKNPGYYDIEAYNLGVWHVPNKTPLSVWRNSSLQRYRTTDGILFKHG
HP HNLPGIYQKYPVKYGECKCWTDNQGPVIVVYDFGDAQKTASYSPYQGREFTAGFVQFRV
  * * * * * . ***** * * * * * . ***** * * * * *
XL GNLFSLYRIYPVKYIGIGSCSKDSGPTVPVVYDLGSARKLTASFYSPDFRSQFTPGYIQFRP
HP FNNERAANALCAGMRVTGCNTEHHCIGGGGYFPEASPPQCGDFSGFDWSGYGVTHVGYSSS
  . * * * * * * * * * * * * * * * * * * * * * * * * * * *
XL INTEKAALALCPGMKMSCNVHVCIGGGGYFPEADPRQCGDFAAYDFNGYGTCKKFNPSAG
HP REITEAAVLLFYR
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XL IEITEAAVLLFYL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R06009) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02515> (SEQ ID Nos. 32, 42, and 52)

Determination of the whole base sequence of the cDNA insert of clone HP02515 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 176-bp 5'-untranslated region, a 690-bp ORF, and a 71-bp 3'-untranslated region. The ORF codes for a protein consisting of 229 amino acid residues and there existed a putative secretory signal at N-terminus and one putative transmembrane domain at the C-terminus. Figure 12 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was almost identical with the molecular weight of 26,000 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 25.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from phenylalanine at position 28.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human T1/ST2 receptor binding protein (GenBank Accession No. U41804). Table 7 shows the

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HP  MGDKIWLFPFVLLLAALFPVLLPGAAGFTPSLSDSFTFTLPAGQKECFYQPMPLKASLE
      *... ** .*** . ** * . *... ** ***.**.*. * .***
T1  MMAAGAALALALWLL--MPFVEV--GGAGPPP IQDGEFTFLPAGRKQCFYQSAPANASLE
HP  IEYQVLGDGAGLIDPHLASPEGKTLVFEQRKSDGVHVTVE--TEVGDMYFCFDNFTSTISEK
      .****.*****.* *.*.* ** * **.****** **.***.*.*****
T1  TEYQVIGGAGLVDVDTLESPPQGVLLVSESRKADGVHVTVEPTAGDYKLCFDNSFSTISEK
HP  VIFFELILDNMGEQAQEDEDWKYITGTDILDMKLEIDILESINSIKSRLSKSGHIQILLR
      ..*****.*.. ..*.*. . .**.*.*** **.*.....*..*..***
T1  LVFFELIFDSL--QDDEEVEGWAEAVEPEEMLDVKMEDIKESIETMRTRLRSIQMLTLRL
HP  AFEARDNRNIQESNFDNRVFNWVMVNLVVMVVVSAIQVYMLKSLFPEDKRKRST
      *****.*.*.*.*****.*.*.*.*.*.*.*.*.*.*
T1  AFEARDNLOEGNLERVFNWFSAVNVAUULLLVAVLQVCTLRKFPQDKRPVPT

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA381943) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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&lt;HP02575&gt; (SEQ ID Nos. 33, 43, and 53)

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Determination of the whole base sequence of the cDNA insert of clone HP02575 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1404-bp ORF, and a 219-bp 3'-untranslated region. The ORF codes for a protein consisting of 467 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 13 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 52 kDa that was almost identical with the molecular weight of 54,065 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 57 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exist in the amino acid sequence of this protein three sites at which N-glycosylation may occur (Asn-Arg-Thr at position 171, Asn-Ser-Thr at position 239 and Asn-Asp-Thr at position 377). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from histidine at position 29. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the supernatant fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human  $\alpha$ -L-fucosidase (SWISS-PROT Accession No. P04066). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human  $\alpha$ -L-fucosidase (FC). Therein,

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N28668) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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10 <HP10357> (SEQ ID Nos. 34, 44, and 54)

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Determination of the whole base sequence of the cDNA insert of clone HP10357 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 113-bp 5'-untranslated region, a 300-bp ORF, and a 54-bp 3'-untranslated region. The ORF codes for a protein consisting of 99 amino acid residues and there existed two putative transmembrane domains. Figure 14 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 11 kDa that was almost identical with the molecular weight of 10,923 predicted from the ORF.

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25 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA477156) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10447> (SEQ ID Nos. 35, 45, and 55)

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Determination of the whole base sequence of the cDNA

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insert of clone HP10447 obtained from cDNA library of human liver revealed the structure consisting of a 271-bp 5'-untranslated region, a 570-bp ORF, and a 34-bp 3'-untranslated region. The ORF codes for a protein consisting of 189 amino acid residues and there existed five putative transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA296976) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10477> (SEQ ID Nos. 36, 46, and 56)

Determination of the whole base sequence of the cDNA insert of clone HP10477 obtained from cDNA library of human liver revealed the structure consisting of a 149-bp 5'-untranslated region, a 1092-bp ORF, and a 15-bp 3'-untranslated region. The ORF codes for a protein consisting of 363 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,884 predicted from the ORF.

The search of the protein data base using the amino

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

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of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10513> (SEQ ID Nos. 37, 47, and 57)

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Determination of the whole base sequence of the cDNA insert of clone HP10513 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 134-bp 5'-untranslated region, a 750-bp ORF, and a 0-bp 3'-untranslated region. The ORF codes for a protein consisting of 249 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 27,373 predicted from the ORF.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0512 (GenBank Accession No. AB011084). Table 10 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0512 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 31.6% in the C-terminal region of 196 amino acid residues.

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consisting of a 47-bp 5'-untranslated region, a 297-bp ORF, and a 245-bp 3'-untranslated region. The ORF codes for a protein consisting of 98 amino acid residues and there existed two putative transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CEF49C12.12 (GenBank Accession No. Z68227). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CEF49C12.12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.1% in the entire region.

Table 11

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25	HP M-ASLLCCGPRLAACGIVLSAWGVIMLIMLGIPFNVHSAVLIEDVPPTKDPENGPNQNIY
	*        ***   *   *   *   *   *   *   *   *   *   *   *   *
	CE MGKICPLMGPKMSAPCMVMSVWGVIFLGLLGVPFYIQAVTLFPDLHF-EGHGKVPSSVID
45	HP NLYEQVSYNCFIAAGLYLLGGFSFCQVRLNKRKEYMVR
	*        *   *   *   *   *   *   *   *   *
30	CE AKYNEKATQCWIAAGLYAVTLIAVFWQ---NKYNTAQIF

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA420715) in ESTs; but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

10 <HP10557> (SEQ ID Nos. 39, 49, and 59)

Determination of the whole base sequence of the cDNA insert of clone HP10557 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 24-bp 5'-untranslated region, a 519-bp ORF, and a 130-bp 3'-untranslated region. The ORF codes for a protein consisting of 172 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was larger than the molecular weight of 18,844 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 39 kDa which is considered to have been subjected to some modification after secretion. In addition, there exist in the amino acid sequence of this protein no site at which N-glycosylation may occur. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 32. When expressed in COS7 cells, an expression product of about 20 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human progesterone binding protein (EMBL Accession No. AJ002030). Table 12 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human progesterone binding protein (PG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.5% in the C-terminal region of 151 amino acid residues.

Table 12

HP	MVGPAP
PG MAAGDGDVKGTLGSGSESSNDGGSESPGDAGAAAEGGGWAAAALALLTGGGEMLLNVAL	
HP RRRRLRPLAALALVLALAPGLPTARAGQTPRPAERGPPV--RLFTEEELARYGGEEDQPI	
PG VALVLLGAYRLWVRWGRRGLGAGAGAGEESPATSLPRMKRDFSLQLRQYDG--SRNPRI	
HP YLAVKGVVFDVTSGREFYGRGAPYNALTGKDSTRGVAKMSLDPADLTHDTTGLTAKELEA	
PG LLAVNGKVFDVTKGSKFYGPAGPYGIFAGRDASRGLATFCLDKDALRDEYDDLSDLNAVQ	
HP LDEV--FTKVYKAKYPIVGYTARRILNEDGSPNLDKPEDQPHFDIKDEF	
PG MESVREWEMQFKEY---DYVG-RLLEKPGGEPS-EYTDEEDTKDHNKQD	

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AAL01709) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10563> (SEQ ID Nos. 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10563 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 126-bp 5'-untranslated region, a 363-bp ORF, and a 936-bp 3'-untranslated region. The ORF codes for a protein consisting of 120 amino acid residues and there existed two putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18.5 kDa that was larger than the molecular weight of 13,180 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein F27F23.15 (GenBank Accession No. AC003058). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the A. thaliana hypothetical protein F27F23.15 (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.5% in the entire region.





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Table 14

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acid sequence of the present protein revealed that the protein was similar to the rat Sec22 homologue (GenBank Accession No. U42209). Table 14 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat Sec22 homologue (RN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 94.6% in the N-terminal region of 241 amino acid residues. The protein of the present invention was longer by 53 amino acids at the C-terminus than the rat Sec22 homologue.

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HP	MSMILSASVIRVRDGLPLSASTDYEQSTGMQECRKYFKMLSRKLAQLPDRCTLKTGHYNI
	*****.*****.***.*.*****.*****..**
RN	MSMILSASVVRVRDGLPLSASTDCEQSAGVQECRKYFKMLSRKLAQFPDRCTLKTGRHNI
HP	NFISSLGVSYYMLCTENYPNVLAFSFLDELQKEFITTYNMMKTNNTAVRPYCFIEFDNFIQ
	*****
RN	NFISSLGVSYYMLCTENYPNVLAFSFLDELQKEFITTYNMMKTNNTAVRPYCFIEFDNFIQ
HP	RTKQRYNNPRSLSTKINLSDMQTEIKLRPPYQISMCELGSAANGVTSAPSVDCGAGAKISS
	*****.*****.*****
RN	RTKQRYNNPRSLSTKINLSDMQMEIKLRPPYQIPMCELGSAANGVTSAPSVDCGAGAKISS
HP	AHQRLPATLSGIVGFILSLLCGALNLIRGFHAIESLLQSDGDDFNIIIAFFLGTAACTLY
	*****.*****.***.*.*****
RN	AHQRLPATLSGIVAFILSLLCGALNLIRGFHAIESLLQSDGEDFSYMIAFFLGTAACTLY
HP	QCYLLVYYTGWRNVKSFLTFLGLICLCNMYLYELRNWLQLFPHVTVGAFVTLQIWLROAQG
	*
RN	QMICLCLQGRKERT

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA421925) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP01956> (SEQ ID Nos. 62, 72, and 82)

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Determination of the whole base sequence of the cDNA insert of clone HP01956 obtained from cDNA library of human liver revealed the structure consisting of a 86-bp 5'-untranslated region, a 552-bp ORF, and a 359-bp 3'-untranslated region. The ORF codes for a protein consisting of 183 amino acid residues and there existed one putative transmembrane domain. Figure 22 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20.5 kDa that was almost identical with the molecular weight of 20,073 predicted from the ORF.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the yeast hypothetical protein 21.5 kDa (SWISS-PROT Accession No. P53073). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the yeast hypothetical protein 21.5 kDa (SC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

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of 34.3% in the C-terminal region of 108 amino acid residues.

Table 15

5	5	HP	MTAQGGGLVANRGRFRKWAIELSGPGGSGRGRSDRSGGQGSLLYPVGYLDKQVPDTS
10			SC MSEQEPYEWAKHLLDTKYIEKYNIQNSNTLPSPGPEGNSSKGNVTRKQDQDTSQTSLA
		HP	VQETDRILVEKRCWDIALGGLKQIPMNLFIMYMAGNTISIFPTMMVCMMAWRPIQALMAI
			. * .. * . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * .
15	10	SC	QKNQITVLQVQKAWQIALQPAKSIPMNIFMSYMSGTSLQIIPINTALMLLSGPIKAIFST
		HP	SATFK--MLESSSQKELQGLVYLIGNLMGLALAV-Y-KCQSMGLLPTHASDWLAFIEPPE
			... * . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * .
20		SC	RSAFKPVLGNKATQSQVQTAMPFYIVFQGVLMYIGYRKLNSMGLIPNAKGDWLPWERIAH
		HP	RMEFSGGGGLLL
25	15	SC	YNNGLQWFSD

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA159753) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP02545> (SEQ ID Nos. 63, 73, and 83)

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Determination of the whole base sequence of the cDNA insert of clone HP02545 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 133-bp 5'-untranslated region, a 984-bp ORF, and a 636-bp 3'-untranslated region. The ORF codes for a

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protein consisting of 327 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 23 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat embigin (EMBL Accession No. AJ009698). Table 16 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat embigin (RN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 65.4% in the entire region.

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osteosarcoma cell line Saos-2 revealed the structure consisting of a 61-bp 5'-untranslated region, a 672-bp ORF, and a 384-bp 3'-untranslated region. The ORF codes for a protein consisting of 223 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was somewhat larger than the molecular weight of 24,555 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 26 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 20.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse FGF binding protein (GenBank Accession No. U49641). Table 17 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse FGF binding protein (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 21.2% in the entire region other than the N-terminal region. In particular, all the eight cysteine residues contained in the both proteins were conserved.

Table 17

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HP                               MKFVPCLLLVTLSCGLTLGQAPRQKQGST
                                ...*...
5  MM MRLHSLILLSFLLLATQAFSEKVRKRAKNAPHSTAEEGVEGSAPSLGKAQNKQRSRTSKS
HP GEEFHFQTGGRDSCMRPSSLGQAGVWLRVDCRNTDQTYWCEYRGQPSMCQAFADPK
    ..*...
MM LTHGKFVTKDQATC---RWAVTEEEQGISLKVQCTQADQEFSCVFAGDPTDCLKHKDKD-Q
HP SYWNQALQELRLHACQGA-PVLRPSVCREAGPQAHMQQVTSSLKGSPEPNQQPEAGTP
10  **...
MM IYWKQVARTLRKQKNICRDAKSVLKTRVCRKRFEPESNLKLVNPNARGNTKPRKEKAEVSA
HP SLRPKATVKLTETATQLGKDSMEELGKAKPTTRPTAKPTQPGPRPGNEEAKKAWHCWK
    ..*...
25  MM REHNKVQEAVSTEPNRIKEDI-TLNPAATQTM-TIRDPECLEDDPVLNQ-RKTALEPCGE
15  HP PFQALCAFLISFFRG
    ..*...
MM SWSSICTFFLNMLQATSC

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA317400) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02631> (SEQ ID Nos. 65, 75, and 85)

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 147-bp ORF,



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and a 1191-bp 3'-untranslated region. The ORF codes for a protein consisting of 48 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa or less.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02632> (SEQ ID Nos. 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP02632 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 50-bp 5'-untranslated region, a 1116-bp ORF, and a 337-bp 3'-untranslated region. The ORF codes for a protein consisting of 371 amino acid residues and there existed eight putative transmembrane domains. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELC2H12 (GenBank Accession No. U23169). Table 18 shows the comparison between amino acid sequences

of the human protein of the present invention (HP) and the C. elegans hypothetical protein CELC2H12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 51.4% in the entire region.

Table 18

10	HP	MAWTRYQLFLAGMLVLTGSINTLSAKWADNFM AEGCGGSKHSFQHPFLQAVGMFLGEFS
		..... *.****.*.....*.....*.....*.....*.....*.....*.....*
25	CE	MVAFAVIISVMVVTGSLNTICAKWADSIKAD-----GVFFNHPFLQATCMFFGRFL
	HP	CLAAFYL-----LRCRAAGQSDS-----SVDPPQPFNPLFLPALCDMTGTSL
15		*...*...*...*...*...*...*...*...*...*...*...*...*...*
	CE	CLVVFFLIFGKYVWNRANVQGESGVSVEITSEEKPTLPFFNPLFLPPPALCDILGTSI
30	HP	MYVALNMTSASSFQMLRGAVIIFTGLFSVAFGLGRRLVLSQWLGLATL IAGLVVVGGLDLL
		*...*...*...*...*...*...*...*...*...*...*...*...*...*
	CE	MYIGLNLTTASSFQMLRGAVIIFTGLLSVGMLNAQIKPPKWFVMLGLVIVGVTDIY
20	HP	SKHDSQHKLSEVITGDLLIIMAQIIVAIQMVLEEKFVYKHNVHPLRAVGTEGLPGFVILS
35		*...*...*...*...*...*...*...*...*...*...*...*...*...*
	CE	YDDPLDDKNAIITGNLLIVMAQIIVAIQMVYEQKYLTKYDVPALFAVGLEGLFGMVTLS
	HP	LLLVPMYYIPAG-SFSGNPRGTLEDALDAFCQVGQQLIAVALLGNISSIAFFNFAGISV
		*...*...*...*...*...*...*...*...*...*...*...*...*...*
40	25	CE ILNIPFYYIHVPRTFSTNPEGRLEDVIFYAWKEITEEPTIALALSGTVVSIAPFPAGVSV
	HP	TKELSATTRMVLDSLRTVVIWALSALGWAFHALQILGFLILLIGTALYNGLHRPLLGR
		*...*...*...*...*...*...*...*...*...*...*...*...*...*
	CE	TKELSATTRMVLDSVRTLVIVVVSIPLFHEKFAIQLSGFAMLI LGTLIYNDILIGPWFR
45	HP	LSRGRPLAESEQRLLGGTRTPINDAS
	30	CE RNILPNLSSHANCARCWLCICGGDSELIEYEQEDQEHLEA

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N50907) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10488> (SEQ ID Nos. 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10488 obtained from cDNA library of human liver revealed the structure consisting of a 39-bp 5'-untranslated region, a 273-bp ORF, and a 421-bp 3'-untranslated region. The ORF codes for a protein consisting of 90 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,151 predicted from the ORF. When expressed in COS7 cells, an expression product of about 6 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H73534) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10538> (SEQ ID Nos. 68, 78, and 88)

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Determination of the whole base sequence of the cDNA insert of clone HP10538 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 357-bp 5'-untranslated region, a 1500-bp ORF, and a 1911-bp 3'-untranslated region. The ORF codes for a protein consisting of 499 amino acid residues and there existed at least four putative transmembrane domains. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse pore-forming K<sup>+</sup> channel subunit (GenBank Accession No. AF056492). Table 19 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse pore-forming K<sup>+</sup> channel subunit (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 32.4% in the N-terminal region of 241 amino acid residues.

Table 19

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HP  MVDRCPLLTSIAIFYLAIGAAIFEVLEEPHWKEARKNYVTQKLELLKEFPCLGQEGLDK
      * . . . . . * . . . . . * . . . . . * . . . . . * . . . . .
5  MM MRSTLLALLLVLLYLVS GALVFQALEQPHEQQAQKKMDHGRDQFLRDHPCVSQKSLED
HP  ILEVVS DAAGQG-----VAITGNQTFNNWNWPNAMIFAATVITTIGYGNVAPKTPAGRLF
      . . . . . * * * . . . . . * . . . . . * . . . . . * . . . . .
MM  FIKLLVEALGGGANPETSWTNSSNHSSANWLGSAFFPSGTIIITTIGYGNIVLHETDAGRLF
HP  CVFYGLFGVPLCLTWISALGKFFGGRAKR----LGQPLTKRGVSLRKAQITCTVIFIVWG
10 * . . . . * . . . . * . . . . * . . . . * . . . . * . . . . *
MM  CIFYALVGIPFLFGMLLAGVGDRLGSSLRRGIGHIEAIFLKWHPGGLVRSLSAVLELLIG
HP  VLVHLVIPPFVFMVTEGWNYIEGLYYSPITISTIGFGDFVAGVNPSSANYHALYRYPVELW
      * . . . . * . . . . * . . . . . * . . . . . * . . . . . * . . . .
25 MM  CLLFVLTPTFVFSYMSWSKLEAIYFVIVTLTTVGFDYVPG-DGTGQNSPAYQPLVWFW
15 HP  IYLGlawLSLFVNWKVS MFVEVHKAIKRRRRRRKESFESSPHSRKALQVKGSTASKOVNI
      * . . . . .
MM  ILFGLAYFASVLTIGNWLRVSRRTAEMGGLTAQAASWTGTVTARVTQRTGFSAPFPE

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R25184) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10542> (SEQ ID Nos. 69, 79, and 89)

Determination of the whole base sequence of the cDNA insert of clone HP10542 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 23-bp 5'-untranslated region, a 321-bp ORF, and a 426-bp 3'-

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untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 29 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,724 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA029683) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10571> (SEQ ID Nos. 70, 80, and 90)

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Determination of the whole base sequence of the cDNA insert of clone HP10571 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 95-bp 5'-untranslated region, a 459-bp ORF, and a 675-bp 3'-untranslated region. The ORF codes for a protein consisting of 152 amino acid residues and there existed one putative transmembrane domain. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20 kDa that was larger than the molecular weight of 17,062 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 23 kDa

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which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ile-Thr at position 10).

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5 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA105822) in ESTs, but, since they are partial sequences, it can not be judged whether or not 10 any of these sequences codes for the same protein as the protein of the present invention.

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<HP01470> (SEQ ID Nos. 91, 101, and 111)

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15 Determination of the whole base sequence of the cDNA insert of clone HP01470 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 157-bp 5'-untranslated region, a 1077-bp ORF, and a 385-bp 3'-untranslated region. The ORF codes for a protein consisting of 358 amino acid residues and there existed one putative 20 transmembrane domain. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro 35 translation resulted in formation of a translation product of 43 kDa that was somewhat larger than the molecular weight of 40,489 predicted from the ORF. In this case, the addition 40 of a microsome led to the formation of a product of 40 kDa from which the secretory signal is considered to have been cleaved and a product of 43.5 kDa which is considered to 45 have been subjected to some modification. Application of the 30 (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the 50 mature protein starts from glycine at position 23. When

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expressed in COS7 cells, an expression product of about 44 kDa was observed in the supernatant fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein 39.9 kDa (SWISS-PROT Accession No. Q10005). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein 39.9 kDa (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 58.9% in the entire region.

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Table 20

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HP MAPQNLSTFCLLLLYLIGAVIAGRDPFYKILGVPRASIKDIKKAYRKALQLHPDRNPDD
      *.. * *****...* ..***** ..*****..*
5 CE MRILNVSLVASSLVAFVECGRDPFYKILGVAKNANANQIKKAYRKALAKELEHPDRNQDD
HP PQAQEKFDLGAAYEVLSDSEKQYDTYGEGL--KDGHQSSHGDIFSHFFGDFGFMFG
      *..*****..*****..* ..*****..* ..* ..* ..* ..* ..* ..* ..*
15 CE EMANEKFQDLSSAYEVLSDKEKRAMYDRHGEEGVAKMGGGGGGGHDPFSSFFGDF-FG-G
HP GTPRQQRNIPRGSDIIVDLVTLLEVYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTT
      *..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..*
10 CE GGGHGGEGTTPKGADVTIDLVTLLEVYNGHFVEIKRKKAVYKQTSGRQCNCRHEMRTE
HP QLGPRGFQMTQEVVCECPNVKLVNEERTLEVEIEPGVRDGMETPFGEPEPHVDGEPGD
      *..***** * ..*****..*****..* ..* ..* ..* ..* ..* ..* ..*
25 CE QMGQGRFQMFQVKVCECPNVKLVQENKVLVEVEVGADNGHQQIFHGEPEPHIEGDPGD
HP LRFRIKVVKHPIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVVHISRDKITRPGAK
      *..*.. *..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..*
15 CE LKFKIRIQKHPFRERKGGDDLYTNVTISLQDALNGFEMEIQHLOGHIVKVRDKVTWPGAR
HP LWKKGEGLPNFDNNNIKGLIITFDVDFPKEQLTEEAREGIKQLLKQGSVQ-KVYNGLQG
      *..*..*..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..* ..*
20 CE LRKKDEGMPSLEDNNKGMVLVTFDVEFPKTELSDEQKAQIIEILQQNTVKPRAYNGL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282838) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30 <HP002419> (SEQ ID Nos. 92, 102, and 112)

Determination of the whole base sequence of the cDNA insert of clone HP02419 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 253-bp

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5'-untranslated region, a 681-bp ORF, and a 1120-bp 3'-untranslated region. The ORF codes for a protein consisting of 226 amino acid residues and there existed four putative transmembrane domains. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0108 (SWISS-PROT Accession No. Q15012). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0108 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.9% in the entire region.

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of the translation product and the sequence comparison data with the *Caenorhabditis elegans* homologue. The ORF codes for a protein consisting of 195 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 58 kDa. In this case, the addition of a microsome led to the formation of a product of 56 kDa from which the secretory signal is considered to have been cleaved. Since both of these products are larger than the molecular weight of 22 kDa predicted from the ORF, it is likely that the protein interacts with another protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein C35C5.3 (EMBL Accession No. Z78417). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein C35C5.3 (CE). U at position 49 in the amino acid sequence of the protein of the present invention represents selenocysteine. Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.9% in the entire region other than the N-terminal region. Cystein was found in the sequence of the *C. elegans* protein at the position corresponding to position 49 encoded by the stop codon (selenocysteine) of the protein of the present invention.

Table 22

HP	MRLLLL
5	CE MRIHDELQKQDMSRFGVFIIGVLPFMSVCDVLRTEESHSDENHVHEXDDFPAEFGDETDS
15	HP LLVAASAMVRSEASANLGGVPSKRLKMQYATGPLLKFKICVSUGYRRVPFEYMRVISQRY
	* ... *** **...*... *
	CE QSPSQGTEEDHIEVREQSSFVKPTAVHHAKDLPTLRIPYCVSCGYKQAFDQPTTFAKEY
20	HP PDIRIEGENYLPQPIYRHIASFVSVFKLVLIIGLIIVGKDPFAFFGMQAPSIWQWGQENKV
10	*...***.*. * ..* ** *... *..* **.* **.* *...*
	CE PNMPIEGANFAPVLWKAYVAQALSFVKMAVLVLVGGINPFERFGLGYPQILQAHGKMK
25	HP YACMMVFFLSNMIENQCMSTGAFEITLNDVPVWSKLESGHLPMSMQQLVQILDNEMKLNKH
	***.*.*...*. *****. *... ..***.*...* *...*...*
15	CE SSCMLVFMLGNLVEQSLISTGAFEVYLCGNEQIWSKIESGRVPSPQEFMQLIDAQLAVLGK
	HP MDSIPHERS
	CE APVNTESFGEPQQTIV

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02695> (SEQ ID Nos. 94, 104, and 114)

Determination of the whole base sequence of the cDNA insert of clone HP02695 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 112-bp 5'-untranslated region, a 1020-bp ORF, and a 160-bp 3'-

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untranslated region. The ORF codes for a protein consisting of 339 amino acid residues and there existed three putative transmembrane domains. Figure 34 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 38 kDa that was almost identical with the molecular weight of 38,274 kDa predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat hypertension-induced protein S-2 fragment (PIR Accession No. 539959). Table 23 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat hypertension-induced protein S-2 fragment (RN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.3% in the entire region.

Table 23

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HP MNWELLWLLVLCALLLLVQLLRFLRADGDLTLLWAEWQGRPEWELTDMVWVVTGASS

5 HP GIGEELAYQLSKLGVSLVLSARRVHELERVKRRCLENGNLKEKDILVLPDLTDTGSHEA  
 \*\*\*\*.\*\*\*\*\*.\*\*\*.  
 RN VKRRSLENGNLKEKDILVLPDLADTSSHDI  
 HP ATKAVLQEFGRIDILVNNGGMSQRLCMOTSLDVYRKLIENLYLGTVSLTKCVLPHMIER  
 \*\*\*.\*\*\*\*\*... \*\* .\*.\*\*\*.\*\*\*\*\*.\*\*\*.  
 10 RN ATKTVLQEFGRIDILVNNGGVAHASLVENTNMDIPKVLIEVNYLGTVSLTKCFLPHMMER  
 HP KQGKIVTVNSILGIISVPLSIGYCASKHALRGFFNGLRTELATYPGIIVSNICPGPVQSN  
 .\*\*\*\*\*.\*  
 RN NQGKIVVMKS

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15 Furthermore, the search of the GenBank using the base  
 sequences of the present cDNA has revealed the registration  
 of sequences that shared a homology of 90% or more (for  
 example, Accession No. T84331) in ESTs, but, since they are  
 20 partial sequences, it can not be judged whether or not any  
 of these sequences codes for the same protein as the protein  
 of the present invention.

40 <HP10031> (SEQ ID Nos. 95, 105, and 115)

25 Determination of the whole base sequence of the cDNA  
 insert of clone HP10031 obtained from cDNA library of human  
 osteosarcoma cell line Saos-2 revealed the structure  
 consisting of a 55-bp 5'-untranslated region, a 1464-bp ORF,  
 45 and a 649-bp 3'-untranslated region. The ORF codes for a  
 30 protein consisting of 487 amino acid residues and there  
 existed eleven putative transmembrane domains. Figure 35  
 depicts the hydrophobicity/hydrophilicity profile, obtained

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by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELK07H8 (GenBank Accession No. AF047659). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CELK07H8 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.2% in the entire region.

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Table 24

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HP	MDGTETRQRRLDSCGKPGELGLPHPLSTGGLPVAS
5	CE MKGGGGIGDGKKDYQSAVHEGLTTFDQLGIALEDVGKSMDEATATPGGSLFSRVIFRFRN
	HP EDGALRAPESQSVTPKPLETEPSRETAWSIGLQVTVPFMPAGLGLSWAGMLLDYFQHWPV
	*...*... . . . *... . ** ** ****. .**... **.
	CE ENSSLKSRTYDHSNDLVNMSVIPAESYVLPFQVLFPFAVAGLGMVFAGLVLSIVVTWPL
	HP FVEVKDLLTLVPPPLVGLKGNLEMTLASRLSTAANTGQIDDPQEQRVVISSNLALIQVQAT
10	* * . . . *...*...***** ** *... .. . * . ****.*****
	CE FEEIPEILILVPALLGLKGNLEMTLASRLSTLANLGHMDSSKQRKDVVIANLALVQVQAT
	HP VVGLAAVAALLLGVVSREEVDVAKVELLCASSVLTAFLAALFALGVLVVCIVIGARKLG
	**...**.. * * . . . . * * . .****. ** *... ..** ..
15	CE VVAFLASAFAAALAFIPSGDFDWAHGMALCASSLATAACSASLVLSLLMVVIVTSRKYNI
	HP NPDNIATPIAASLGDLTILSILALVSSPFYR-HKDSRYLTPLVCLSPAALTPVWVLIQKQ
	****.*****.***.***. * * . *...*. . * . * * * . ***.
	CE NPDNVATPIAASLGDLTTLTVLAFFGSVFLKAHNTESWLVNVIIVLFLLLLPFWIXIANE
	HP SPPIVKILKFGWFPPIILAMVISSFGGLILSKTVSKQYKGMIFTPVICGVGGNLVAIQT
	. . . * ** *...*.*** **...* . . *... ..** . *****.***.
20	CE NEGTOETLYNGWTPVIMSLISSAGGFIEATV--RRYHSLSTYGPVLNGVGGNLAOVA
	HP SRISTYLMWSAPGVLPQ--MKKFWPNPCSTFCTSEINSMARSVLLLLLVVPGHLIF-FY
	**...*. . . **** . . . * . . . * . *...*****. * *
	CE SRLSTYFHKAGTVGVLNPNWTVSRF-TSVQRAFFSKEWDSRSARVLLLLLVVPGHICFNFL
	HP I-IYLVGQSVINSQ--TFVVLYLLAGLIQVTILLYLAEMVRLTWHQALDPDNHCIPYL
25	* . . . . . * . **..*...*...*... ..* * * . **** ****
	CE IQLPTLTSKNNVTPHGPLFTSLYMIAAIIQVVILLFVCQLLVALLWKWKIDPDNSVIPYL
	HP TGLGDLGTGLLALCFPTDWLLKSKAELGGISELASGPP
	*...***** . **
	CE TALGDLGTGLLFIVFLTTDHPDPKELTSS
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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

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example, Accession No. AA334000) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10530> (SEQ ID Nos. 96, 106, and 116)

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Determination of the whole base sequence of the cDNA insert of clone HP10530 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 80-bp 5'-untranslated region, a 1182-bp ORF, and a 95-bp 3'-untranslated region. The ORF codes for a protein consisting of 393 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 36 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 46 kDa that was somewhat larger than the molecular weight of 44,912 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 45.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 23. When expressed in COS7 cells, an expression product of about 43 kDa was observed in the supernatant fraction and the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein IG002N01 (GenBank Accession No. AF007269). Table 25 shows the comparison between amino acid sequences of the

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human protein of the present invention (HP) and the A.  
thaliana hypothetical protein IG002N01 (AT). Therein, the  
marks of -, \*, and . represent a gap, an amino acid residue  
identical with that of the protein of the present invention,  
5 and an amino acid residue similar to that of the protein of  
the present invention, respectively. The both proteins  
shared a homology of 27.0% in the N-terminal region of 355  
amino acid residues.

Table 25

[illegible]

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA302913) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

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protein of the present invention.

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<HP10541> (SEQ ID Nos. 97, 107, and 117)

Determination of the whole base sequence of the cDNA  
5 insert of clone HP10541 obtained from cDNA library of human  
15 stomach cancer revealed the structure consisting of a 7-bp  
5'-untranslated region, a 591-bp ORF, and a 113-bp 3'-  
untranslated region. The ORF codes for a protein consisting  
20 of 196 amino acid residues and there existed a putative  
secretory signal at the N-terminus. Figure 37 depicts the  
10 hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
Doolittle method, of the present protein. In vitro  
25 translation resulted in formation of a translation product  
of 23 kDa that was somewhat larger than the molecular weight  
15 of 21,553 predicted from the ORF. In this case, the addition  
of a microsome led to the formation of a product of 20 kDa  
30 from which the secretory signal is considered to have been  
cleaved and a product of 23 kDa which is considered to have  
a sugar chain being attached. Application of the (-3,-1)  
35 rule, a method for predicting the cleavage site of the  
secretory signal sequence, allows to expect that the mature  
protein starts from glycine at position 41. In addition,  
there exists in the amino acid sequence of this protein one  
40 site at which N-glycosylation may occur (Asn-Leu-Thr at  
25 position 185).

The search of the protein data base using the amino  
acid sequence of the present protein revealed that the  
45 protein was similar to the human zymogen membrane protein  
(GenBank Accession No. AF056492). Table 26 shows the  
30 comparison between amino acid sequences of the human protein  
of the present invention (HP) and the human zymogen membrane  
50 protein (ZM). Therein, the marks of -, \*, and . represent a

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gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.6% in the C-terminal region of 133 amino acid residues.

Table 26

HP	MWRVPGTTRRPVTGESPGMHRPEAMLLLTALLGGPTWAGKMYGPGGGKYFS-TTEDYD
	*****
ZM	MLTVALLALLCASASGNAIQARSSSYSGEYSGGGKRFSHSGNQLD
HP	HEITGLRVSVGLLLVKSQVKLGDSWDVKLGALGGNTQEVTLQPGEYITKVFVAFQAFIR
	*****
ZM	GPITALRVRVNTYYIVGLQVRYGKVWSDYVGGRRNGDLEEIFLHPGESVIQVSGKYKWLK
HP	GMVMTSKDRYFFGKLDGQISSAYPSQEGQVLVGIYQYQLLGIKISIGFEWN-YPLEEP
	*****
ZM	KLVFVTDKGRYLSFGKDSGTSFNAVPLHPNTVLRFISGRSGSL-IDAIGLEHWDVYPTSCS
HP	TTEPPVNLTYANSPPVGR
ZM	RC

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340605) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10550> (SEQ ID Nos. 98, 108, and 118)

Determination of the whole base sequence of the cDNA

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insert of clone HP10550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 241-bp 5'-untranslated region, a 324-bp ORF, and a 86-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 38 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA348310) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10590> (SEQ ID Nos. 99, 109, and 119)

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Determination of the whole base sequence of the cDNA insert of clone HP10590 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 77-bp 5'-untranslated region, a 1053-bp ORF, and a 180-bp 3'-untranslated region. The ORF codes for a protein consisting of 350 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,285 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of

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43 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Ser at position 144 and Asn-Leu-Thr at position 328).

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA461346) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10591> (SEQ ID Nos. 100, 110, and 120)

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Determination of the whole base sequence of the cDNA insert of clone HP10591 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 232-bp 5'-untranslated region, a 324-bp ORF, and a 844-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,328 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H09424) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein



of the present invention.

<HP01462> (SEQ ID Nos. 121, 131, and 141)

Determination of the whole base sequence of the cDNA insert of clone HP01462 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 121-bp 5'-untranslated region, a 1452-bp ORF, and a 477-bp 3'-untranslated region. The ORF codes for a protein consisting of 483 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 41 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 72 kDa that was larger than the molecular weight of 55,838 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 21.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein ZK1058.4 (EMBL Accession No. Z35604). Table 27 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein ZK1058.4 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.6% in the entire region.

Table 27

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[illegible]

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

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example, Accession No. AA307793) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP02485> (SEQ ID Nos. 122, 132, and 142)

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Determination of the whole base sequence of the cDNA insert of clone HP02485 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 69-bp 5'-untranslated region, a 1005-bp ORF, and a 1672-bp 3'-untranslated region. The ORF codes for a protein consisting of 334 amino acid residues and there existed one putative transmembrane domain. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 38,171 predicted from the ORF. When expressed in COS7 cells, an expression product of about 23 kDa was observed in the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein W01A11.2 (GenBank Accession No. U64852). Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein W01A11.2 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 45.5% in the entire region.

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Table 28

[illegible]

Furthermore, the search of the GenBank using the base  
sequences of the present cDNA has revealed the registration  
of sequences that shared a homology of 90% or more (for  
example, Accession No. D25664) in ESTs, but, since they are  
partial sequences, it can not be judged whether or not any  
of these sequences codes for the same protein as the protein  
of the present invention.

50                   <HP02798> (SEQ ID Nos. 123, 133, and 143)  
                  Determination of the whole base sequence of the cDNA

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insert of clone HP02798 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 31-bp 5'-untranslated region, a 804-bp ORF, and a 301-bp 3'-untranslated region. The ORF codes for a protein consisting of 267 amino acid residues and there existed four putative transmembrane domains. Figure 43 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 30,778 predicted from the ORF. When expressed in COS7 cells, an expression product of about 26 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human DHHC-containing cysteine-rich protein (GenBank Accession No. U90653). Table 29 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human DHHC-containing cysteine-rich protein (DH). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.0% in the intermediate region of 100 amino acid residues. The positions of seven cysteines were conserved between the two proteins. The protein of the present invention also had the DHHC (Asp-His-His-Cys) sequence.

Table 29

HP	MAPWALLSPGVLVRTGHTVLTWGI
5	DH MYKMNICNKPSNKTAPKSVWTAPAQPSGSPSELQGQSRNRNGWSWPPHPLQIVAWLLYL HP TLVLFLHDTLRLQWEEQGELLPLTFLLLVLGSLLLYLAVSLMDPGYVNVQPP-QEELK * * * * *
10	DH PFAVIGFGILVPLLPHEHWVPAGYACMGAIFAGHLVVHLTAVSIDPADDNVRDKSYAGPLP HP EEQTAMVPPAIPLRRCRYCLVLQPLRARHCRECRRCVRRYDHCPWMENCVGERNHPLFV . . . . .
15	DH IFNRSQHAHVIEDLHCNLCNVDVSARSKECSACNKGVCDFDHCKWLNNCVGERNYRLF HP VYLALQLVLLWGLYLAWSGLRFFQPWGLWLRSSGLLPATPLLLSLFSLVASLLLVSHLY . * . * .
20	DH HVSASALLGVLLVLGCHICLRGVLCPHASAHQPTL

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D79050) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10041> (SEQ ID Nos. 124, 134, and 144)

Determination of the whole base sequence of the cDNA insert of clone HP10041 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 12-bp 5'-untranslated region, a 321-bp ORF, and a 286-bp 3'-untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 44 depicts

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the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 12,060 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein K10B2.4 (GenBank Accession No. U28730). Table 30 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein K10B2.4 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 62.1% in the entire region.

Table 30

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HP	MSTNNMSDPRRPKNVLRYP---PPSECNPALDDPTPDYMNLLGMIFSMCGLMLKLKRWCA
	.****.*...**** .. . . .** *.***.*****.....
CE	MQQNGDPRRTNRIVRYKPLDSTANQQQAISEDPLPEYMNVLGMIFSMCGLMIRMKWCS
HP	WVAVYCSFISFANSRSEDTKQMMSSFMLSISAVVMSYLNQNPQMTPPW
	*.*. ** *****.*.*.***.*****.***** *..***
CE	WLALVCSCISFANTRTSDDAKQIVSSEFMLSISAVVMSYLNQNPFIIPPWVTLTQS

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Furthermore, the search of the GenBank using the base

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sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H20098) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10246> (SEQ ID Nos. 125, 135, and 145)

Determination of the whole base sequence of the cDNA insert of clone HP10246 obtained from cDNA library of human epidermoid carcinoma cell line KB revealed the structure consisting of a 110-bp 5'-untranslated region, a 675-bp ORF, and a 79-bp 3'-untranslated region. The ORF codes for a protein consisting of 224 amino acid residues and there existed five putative transmembrane domains. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat smaller than the molecular weight of 25,244 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human putative seven transmembrane domain protein (GenBank Accession No. Y18007). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human putative seven transmembrane domain protein (TM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

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of the protein of the present invention, respectively. The both proteins shared a homology of 93.3% in the entire region.

Table 31

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HP MTLFHFPGNCFALAYFPYPITYKCSGLSEYNAPWKCQAGVTYLFVQLCKMLFLATFFPTW
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TM MTLFHFPGNCFALAYFPYPITYKCTDLSEYNAPWKCQAGVTYLFVQLCKMLFLATFFPTW
HP EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
*****
TM EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
HP VGARGIEFDWKYIQMSIDSNISLVHYIVASAQVWMITRYDLYHTFRPAVLLLMFLSVYKA
*****
TM VGARGIEFDWKYIQMSIDSNISLGPIYIVASAQVWMITRYDLYHTFRPAVLLLMFLRVYKA
HP FVMETFFVHLCSLGSWAALLARAVVTGLLALSTLALYVAVVNVHS
*****
TM FVMETFFVHLCSLGSWAVLMAGVVVKGLLVIRNLAMYVAVVNVHS

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA453931) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10392> (SEQ ID Nos. 126, 136, and 146)

Determination of the whole base sequence of the cDNA insert of clone HP10392 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure

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consisting of a 24-bp 5'-untranslated region, a 777-bp ORF, and a 726-bp 3'-untranslated region. The ORF codes for a protein consisting of 258 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight of 29,623 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 49.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H15999) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention. In addition, partial identity with the hypothetical protein KIAA0384 (Accession No. AB002382) was observed, although the hypothetical protein had a different ORF.

<HP10489> (SEQ ID Nos. 127, 137, and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10489 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 137-bp 5'-untranslated region, a 333-bp ORF, and a 189-bp 3'-untranslated region. The ORF codes for a protein consisting of 110 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 12,010 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262162) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10519> (SEQ ID Nos. 128, 138, and 148)

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Determination of the whole base sequence of the cDNA insert of clone HP10519 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 67-bp 5'-untranslated region, a 276-bp ORF, and a 367-bp 3'-untranslated region. The ORF codes for a protein consisting of 91 amino acid residues and there existed one putative transmembrane domain. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,275 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W16639) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

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of the present invention.

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<HP10531> (SEQ ID Nos. 129, 139, and 149)

Determination of the whole base sequence of the cDNA  
5 insert of clone HP10531 obtained from cDNA library of human  
15 osteosarcoma cell line Saos-2 revealed the structure  
consisting of a 55-bp 5'-untranslated region, a 1035-bp ORF,  
and a 1092-bp 3'-untranslated region. The ORF codes for a  
20 protein consisting of 344 amino acid residues and there  
10 existed five putative transmembrane domains. Figure 49  
depicts the hydrophobicity/hydrophilicity profile, obtained  
by the Kyte-Doolittle method, of the present protein. In  
25 vitro translation resulted in formation of a translation  
product of high molecular weight.

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15 Furthermore, the search of the GenBank using the base  
sequences of the present cDNA has revealed the registration  
30 of sequences that shared a homology of 90% or more (for  
example, Accession No. R50695) in ESTs, but, since they are  
partial sequences, it can not be judged whether or not any  
20 of these sequences codes for the same protein as the protein  
35 of the present invention.

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<HP10574> (SEQ ID Nos. 130, 140, and 150)

40 Determination of the whole base sequence of the cDNA  
25 insert of clone HP10574 obtained from cDNA library of human  
stomach cancer revealed the structure consisting of a 210-bp  
5'-untranslated region, a 1287-bp ORF, and a 1276-bp 3'-  
45 untranslated region. The ORF codes for a protein consisting  
of 428 amino acid residues and there existed a putative  
30 secretory signal at the N-terminus and one putative  
transmembrane domain in the intermediate region. Figure 50  
50 depicts the hydrophobicity/hydrophilicity profile, obtained

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by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 36.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Drosophila melanogaster* GOLIATH protein (SWISS-PROT Accession No. Q06003). Table 32 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *D. melanogaster* GOLIATH protein (DM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The intermediate region of 169 amino acids of the protein of the present invention shared a homology of 41.4% with the N-terminal region of the *D. melanogaster* GOLIATH protein.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA155685) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

## INDUSTRIAL APPLICABILITY

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The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. All of the proteins of the present invention are secreted or exist in the cell membrane, so that they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or the differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for large-scale expression of these proteins. Cells into which these genes are introduced to express these proteins, can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or

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primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished



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through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more

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preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides

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capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table 33 below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

Table 33

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) <sup>‡</sup>	Hybridization Temperature and Buffer <sup>†</sup>	Wash Temperature and Buffer <sup>†</sup>
A	DNA : DNA	≥50	65°C; 1×SSC -or- 42°C; 1×SSC, 50% formamide	65°C; 0.3×SSC
B	DNA : DNA	<50	T <sub>B</sub> *; 1×SSC	T <sub>B</sub> *; 1×SSC
C	DNA : RNA	≥50	67°C; 1×SSC -or- 45°C; 1×SSC, 50% formamide	67°C; 0.3×SSC
D	DNA : RNA	<50	T <sub>D</sub> *; 1×SSC	T <sub>D</sub> *; 1×SSC
E	RNA : RNA	≥50	70°C; 1×SSC -or- 50°C; 1×SSC, 50% formamide	70°C; 0.3×SSC
F	RNA : RNA	<50	T <sub>F</sub> *; 1×SSC	T <sub>F</sub> *; 1×SSC
G	DNA : DNA	≥50	65°C; 4×SSC -or- 42°C; 4×SSC, 50% formamide	65°C; 1×SSC
H	DNA : DNA	<50	T <sub>H</sub> *; 4×SSC	T <sub>H</sub> *; 4×SSC
I	DNA : RNA	≥50	67°C; 4×SSC -or- 45°C; 4×SSC, 50% formamide	67°C; 1×SSC
J	DNA : RNA	<50	T <sub>J</sub> *; 4×SSC	T <sub>J</sub> *; 4×SSC
K	RNA : RNA	≥50	70°C; 4×SSC -or- 50°C; 4×SSC, 50% formamide	67°C; 1×SSC
L	RNA : RNA	<50	T <sub>L</sub> *; 2×SSC	T <sub>L</sub> *; 2×SSC
M	DNA : DNA	≥50	50°C; 4×SSC -or- 40°C; 6×SSC, 50% formamide	50°C; 2×SSC
N	DNA : DNA	<50	T <sub>N</sub> *; 6×SSC	T <sub>N</sub> *; 6×SSC
O	DNA : RNA	≥50	55°C; 4×SSC -or- 42°C; 6×SSC, 50% formamide	55°C; 2×SSC
P	DNA : RNA	<50	T <sub>P</sub> *; 6×SSC	T <sub>P</sub> *; 6×SSC
Q	RNA : RNA	≥50	60°C; 4×SSC -or- 45°C; 6×SSC, 50% formamide	60°C; 2×SSC
R	RNA : RNA	<50	T <sub>R</sub> *; 4×SSC	T <sub>R</sub> *; 4×SSC

‡ : The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

† : SSPE (1×SSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

\*T<sub>B</sub> - T<sub>R</sub> : The hybridization temperature for hybrids anticipated to be less than

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50 base pairs in length should be 5-10°C less than the melting temperature ( $T_m$ ) of the hybrid, where  $T_m$  is determined according to the following equations. For hybrids less than 18 base pairs in length,  $T_m(^{\circ}\text{C}) = 2(\text{\# of A + T bases}) + 4(\text{\# of G + C bases})$ . For hybrids between 18 and 49 base pairs in length,  $T_m(^{\circ}\text{C}) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\% \text{G+C}) \cdot (600/N)$ , where N is the number of bases in the hybrid, and  $[\text{Na}^+]$  is the concentration of sodium ions in the hybridization buffer ( $[\text{Na}^+]$  for  $1\times\text{SSC}=0.165\text{M}$ ).

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Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

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Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

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## Claims

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## CLAIMS

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1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

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2. An isolated DNA coding for the protein according to Claim 1.

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3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140.

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4. The cDNA according to Claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150.

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5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eucaryotic cells.

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6. A transformed eucaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1.

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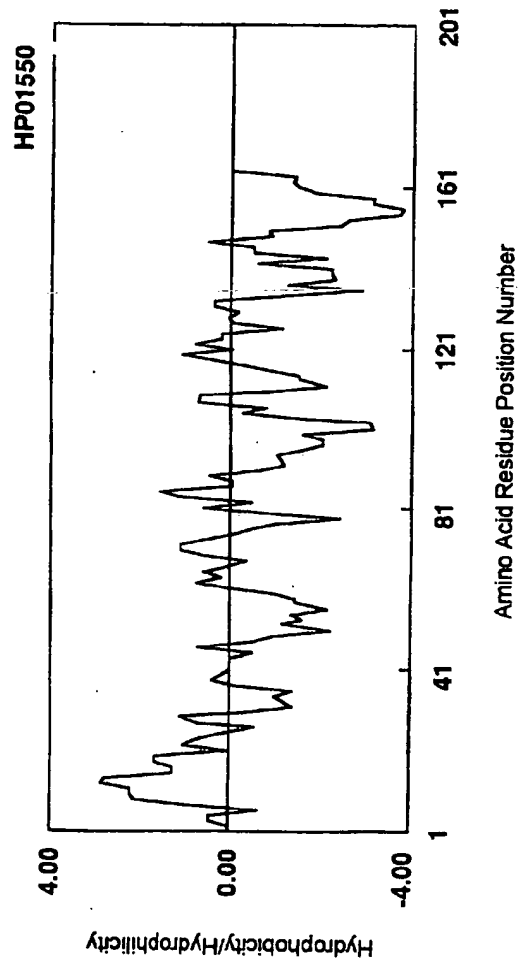


Fig. 1



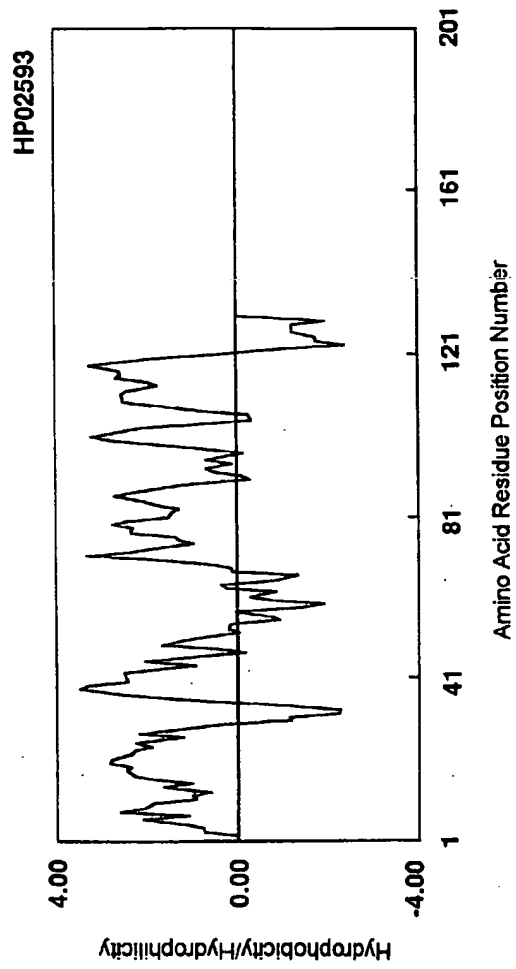


Fig. 2

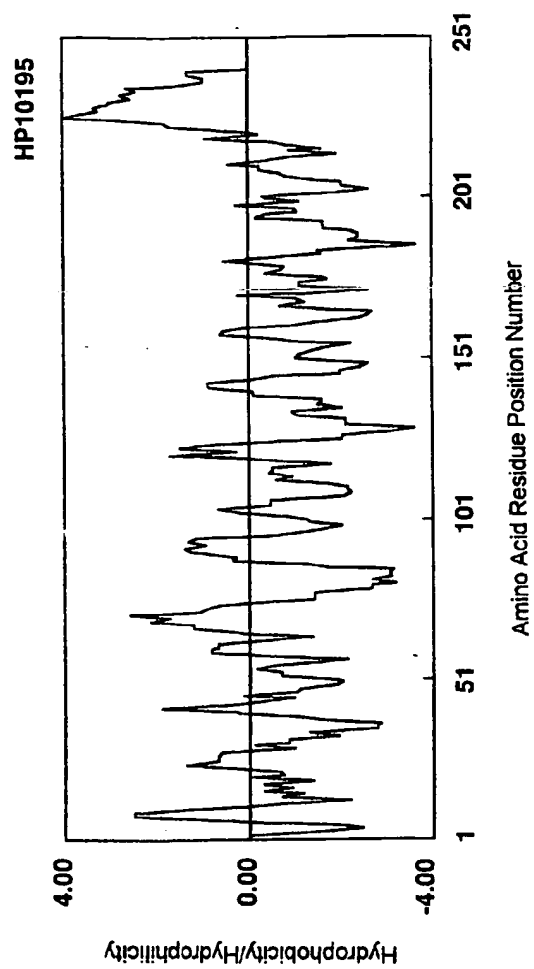


Fig. 3

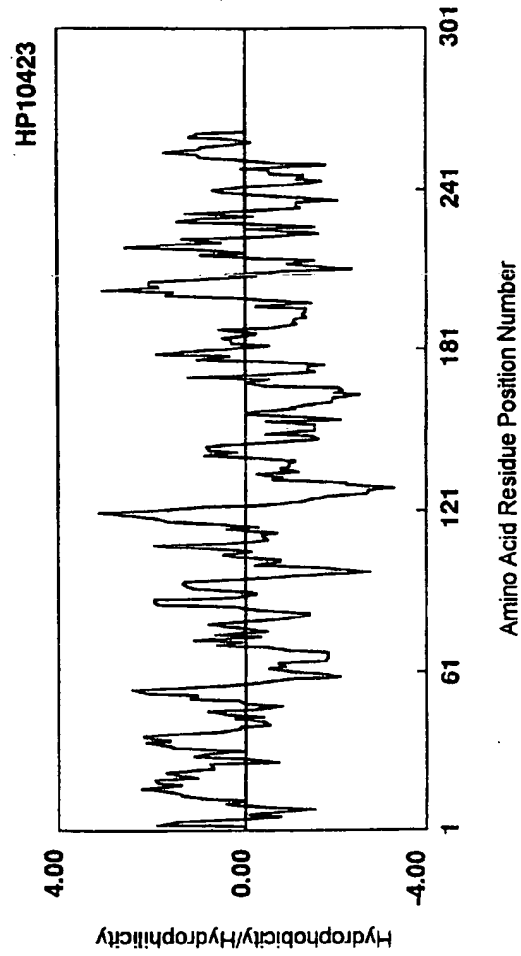


Fig. 4

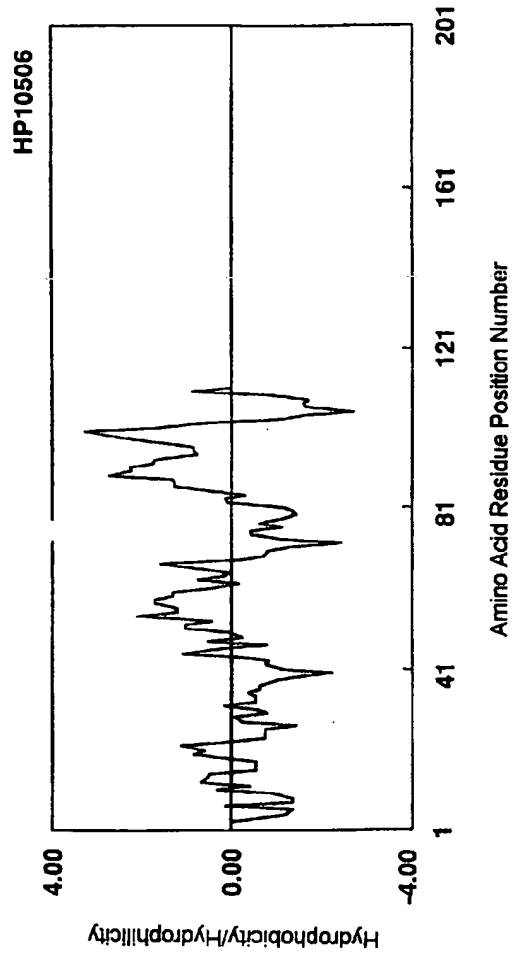


Fig. 5

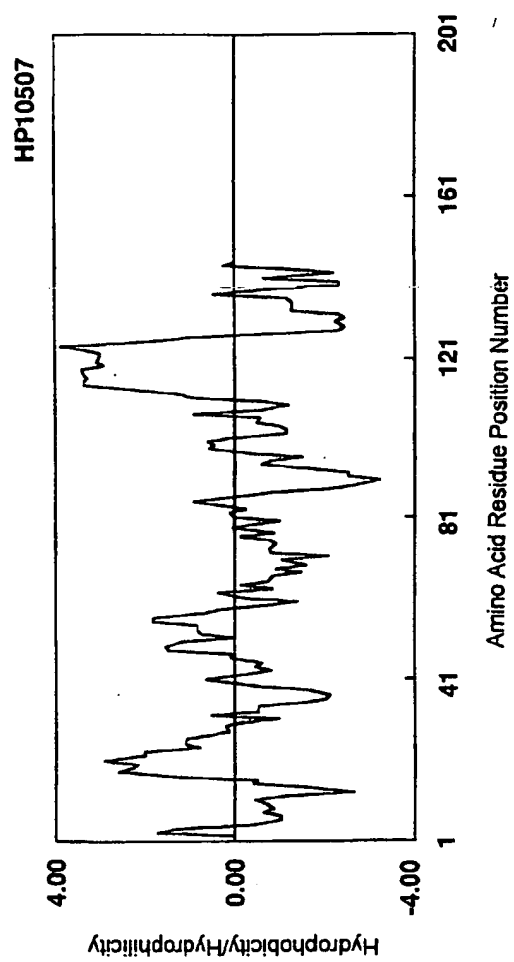


Fig. 6

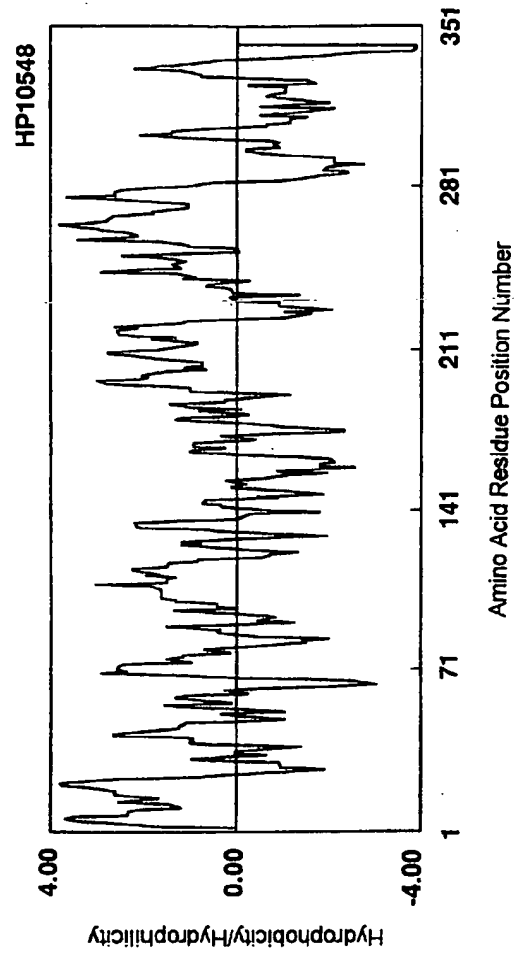


Fig. 7

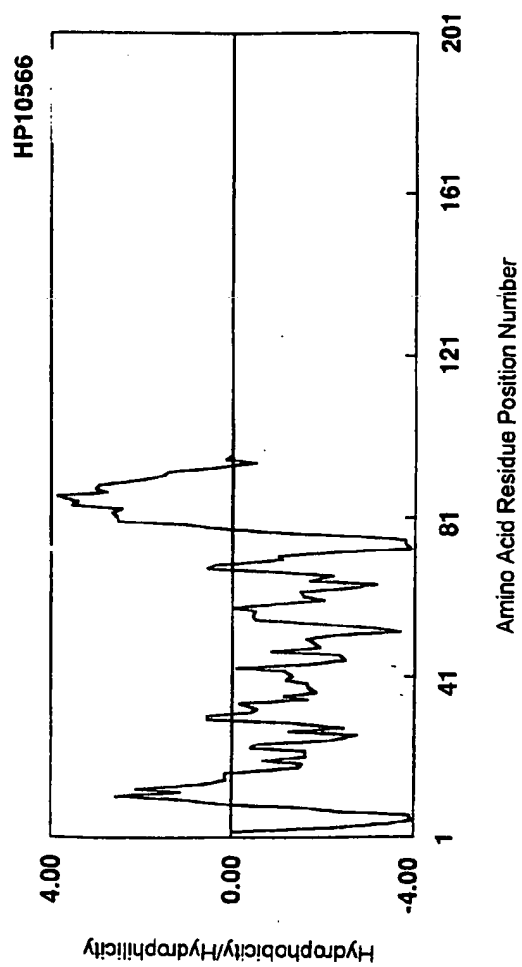


Fig. 8

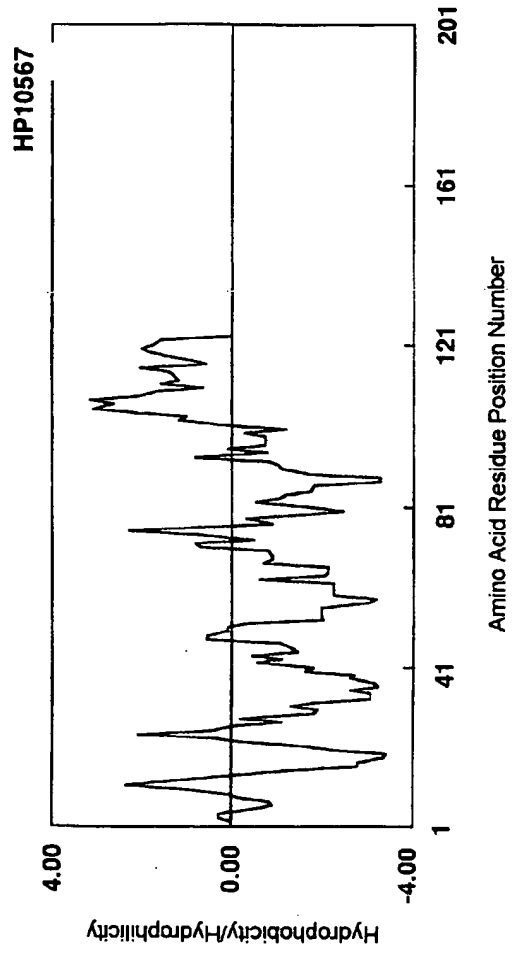


Fig. 9



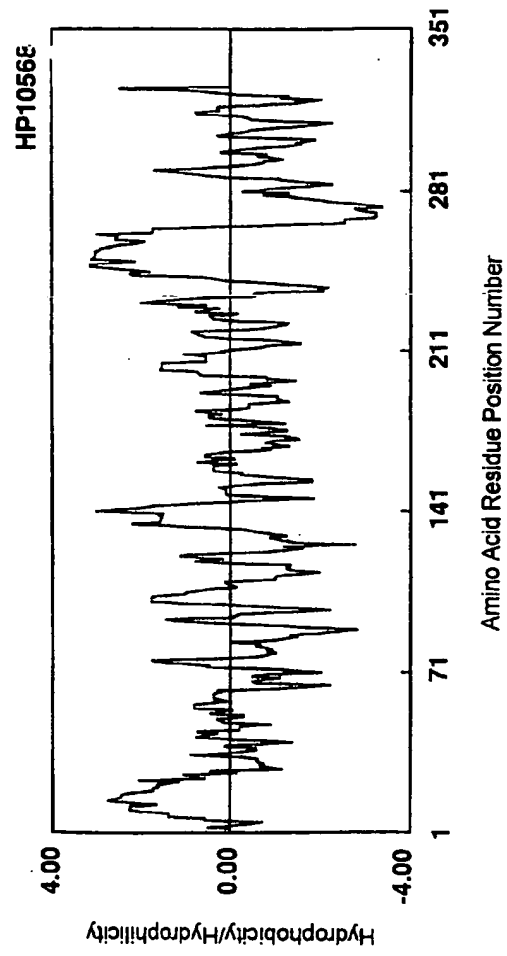


Fig. 10

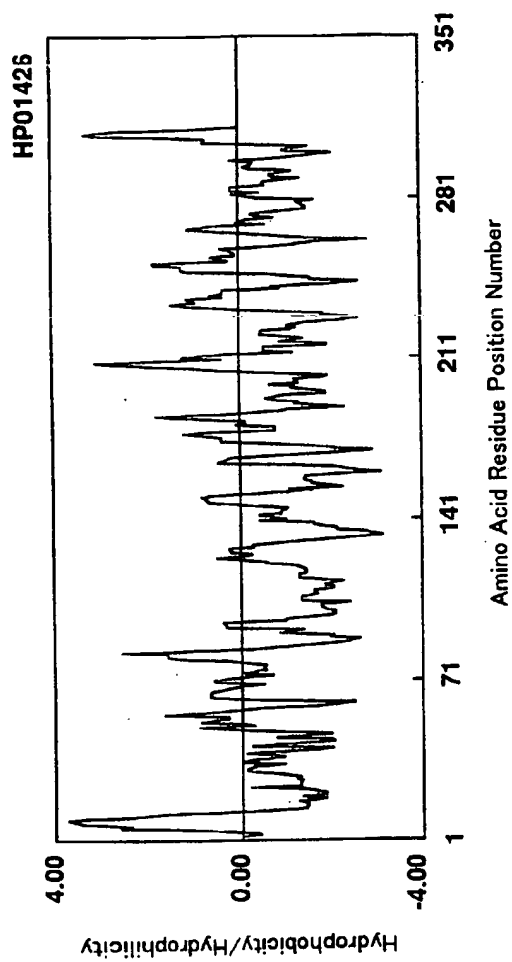


Fig. 11

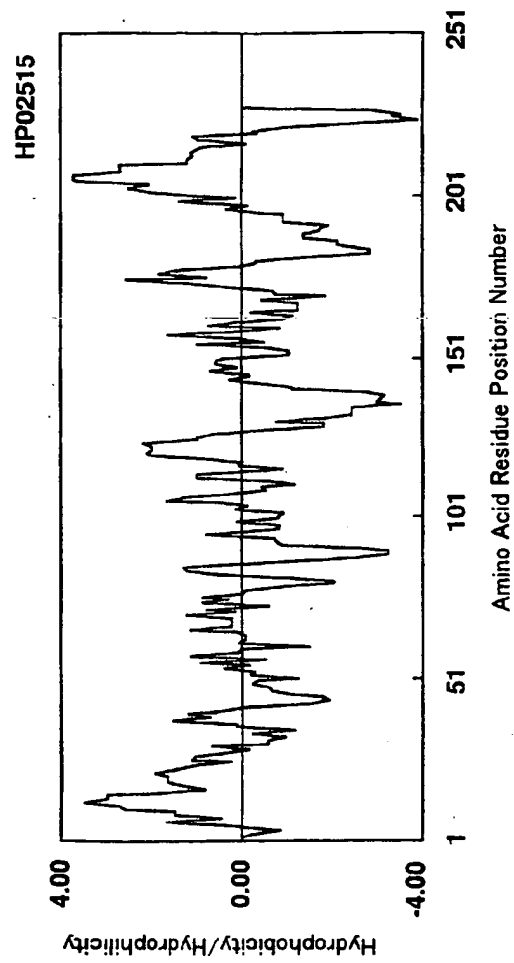


Fig.12

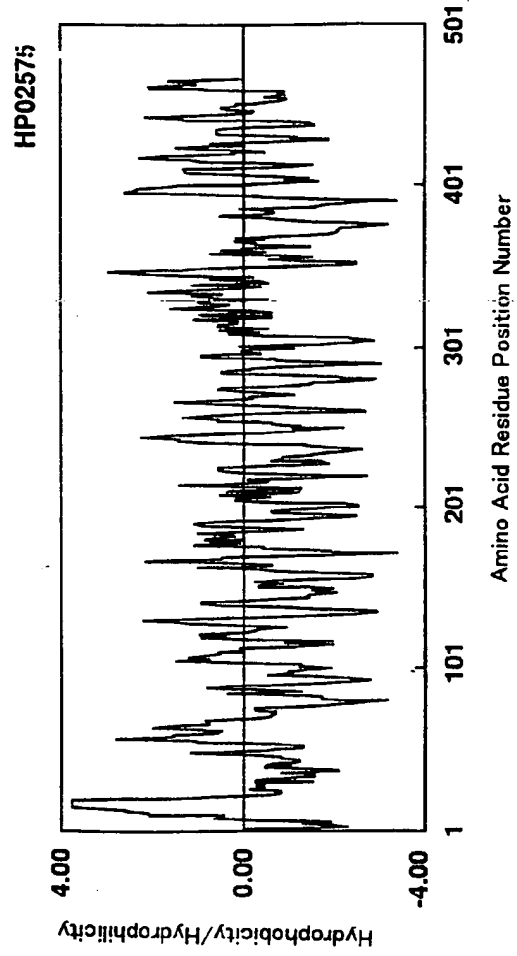


Fig. 13

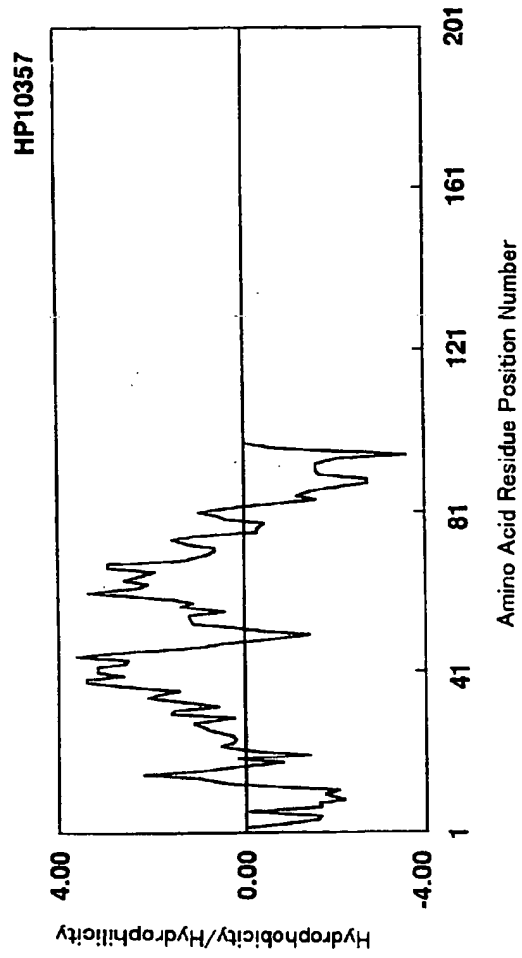


Fig. 14

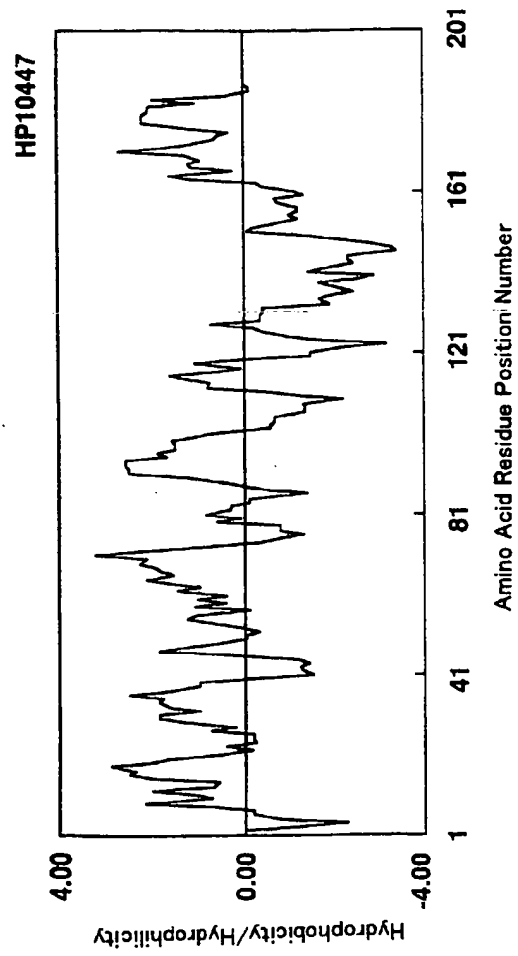


Fig. 15

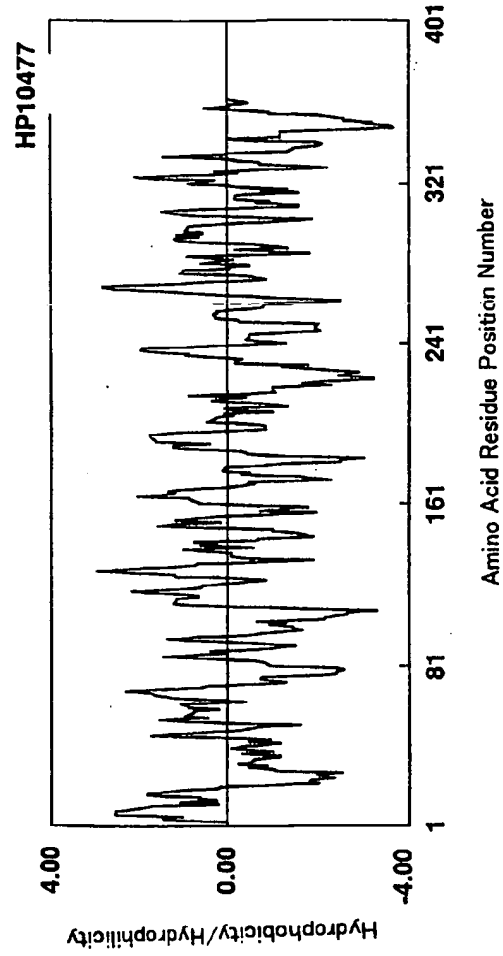


Fig. 16

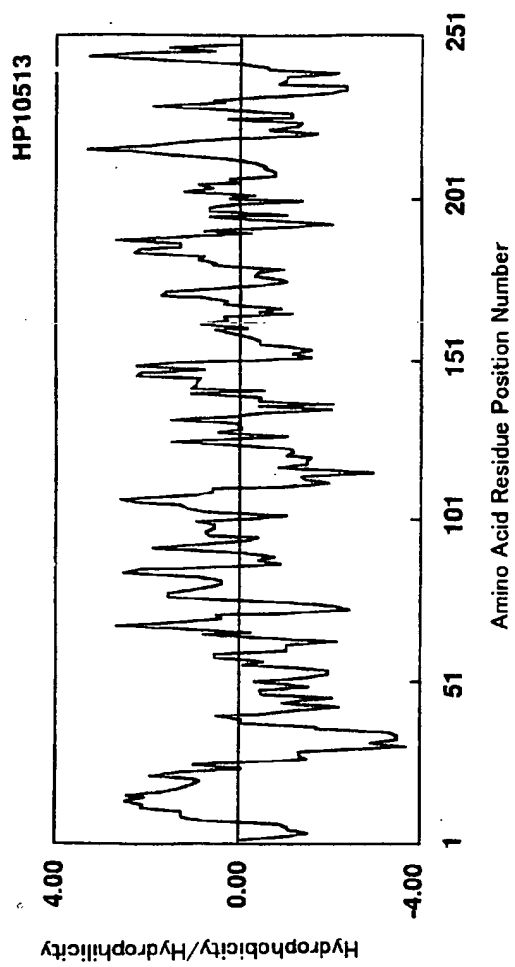


Fig.17



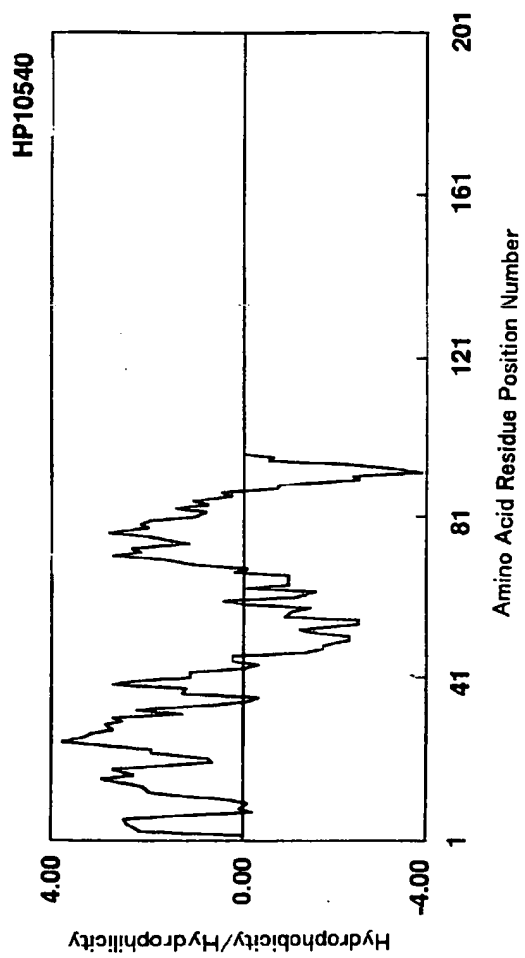


Fig. 18

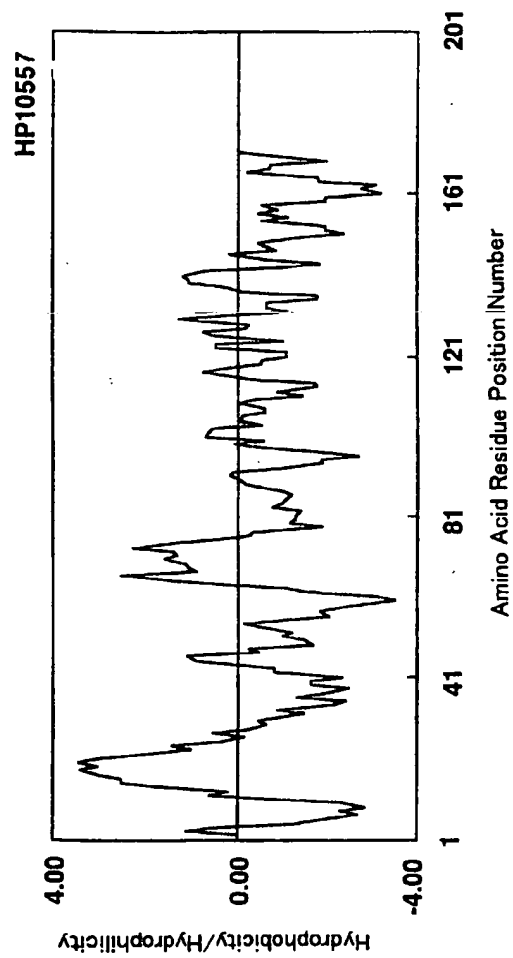


Fig. 19

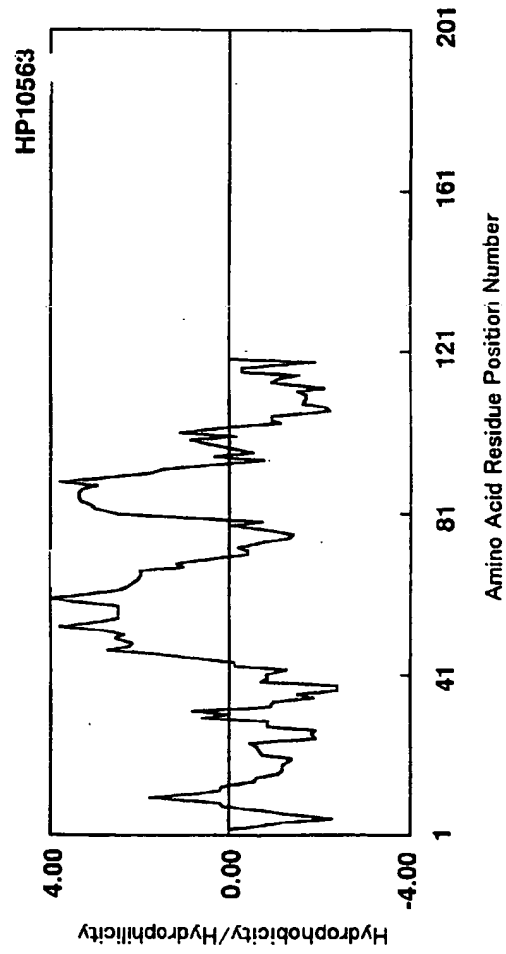


Fig. 20

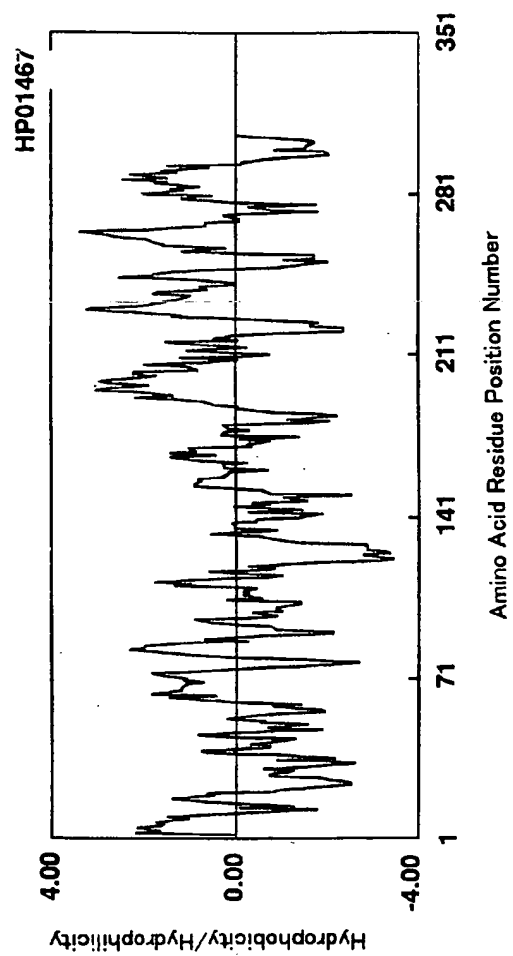


Fig. 21

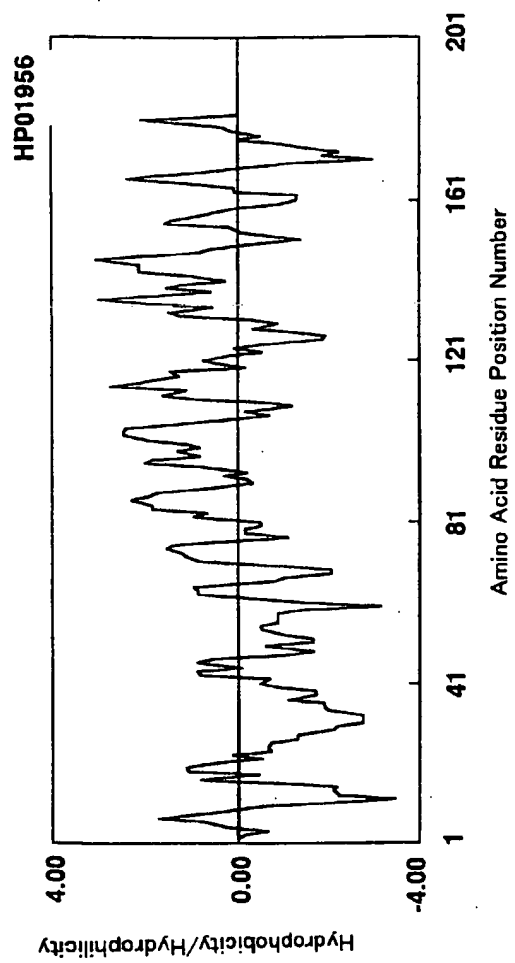


Fig.22

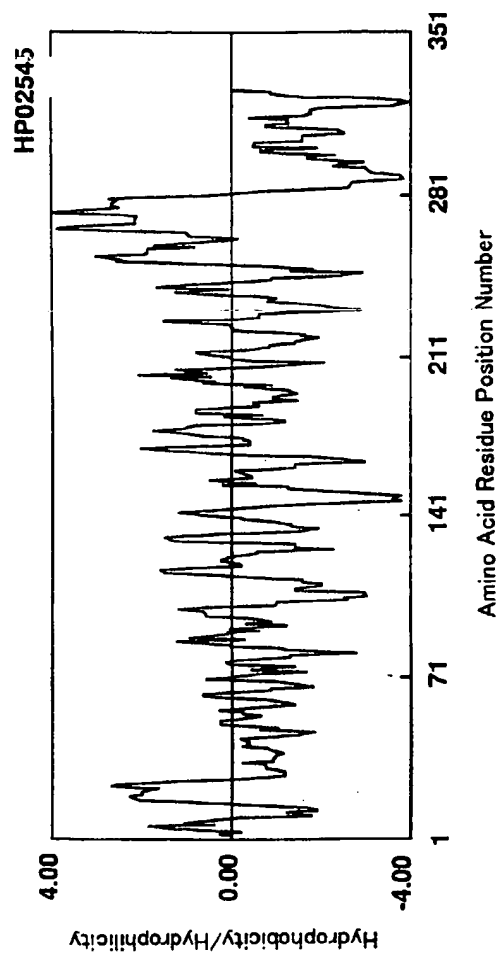


Fig. 23

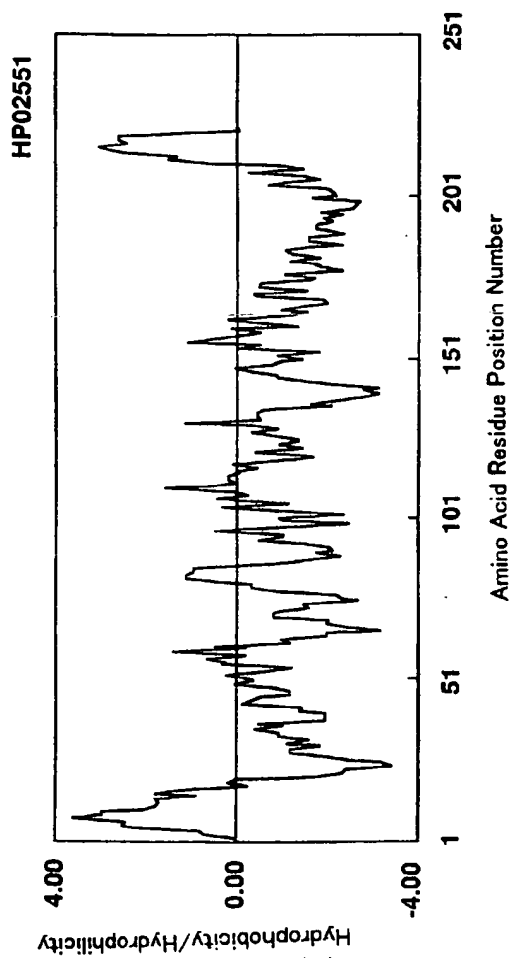


Fig. 24

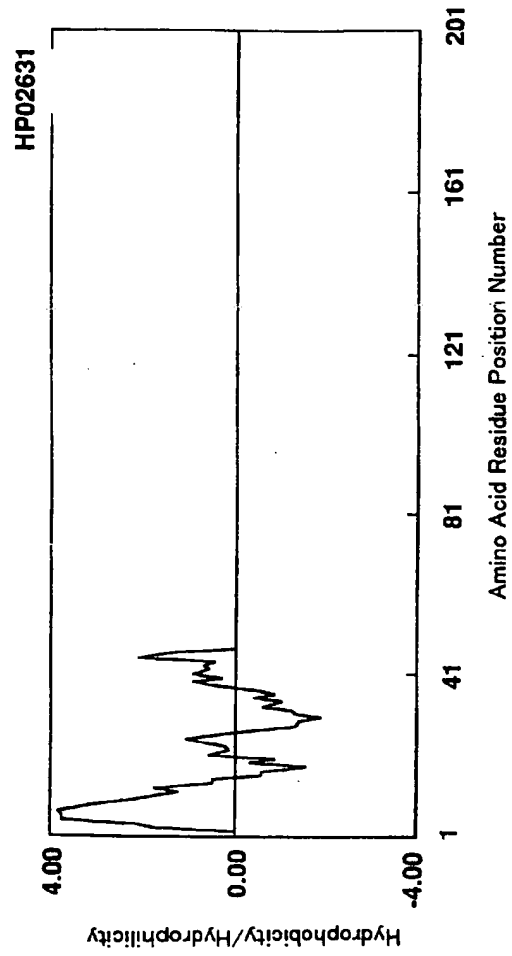


Fig. 25



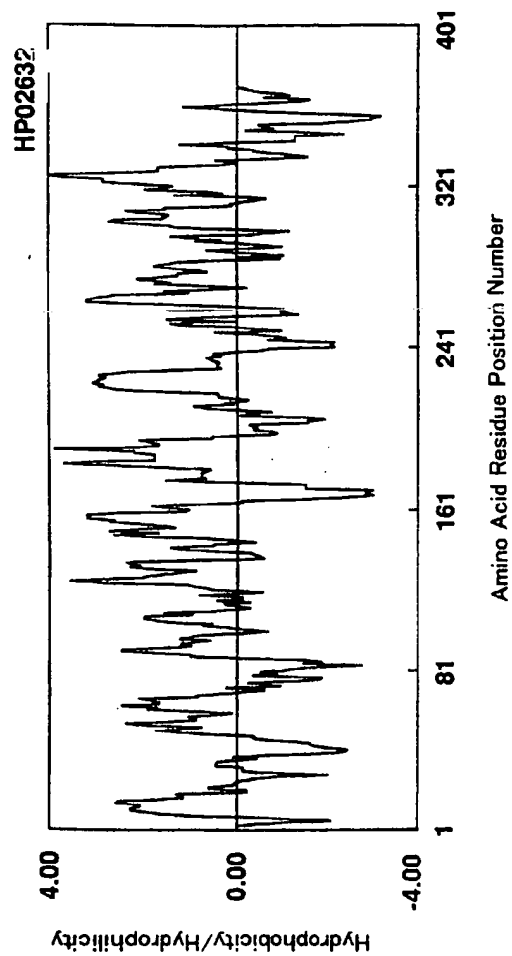


Fig. 26

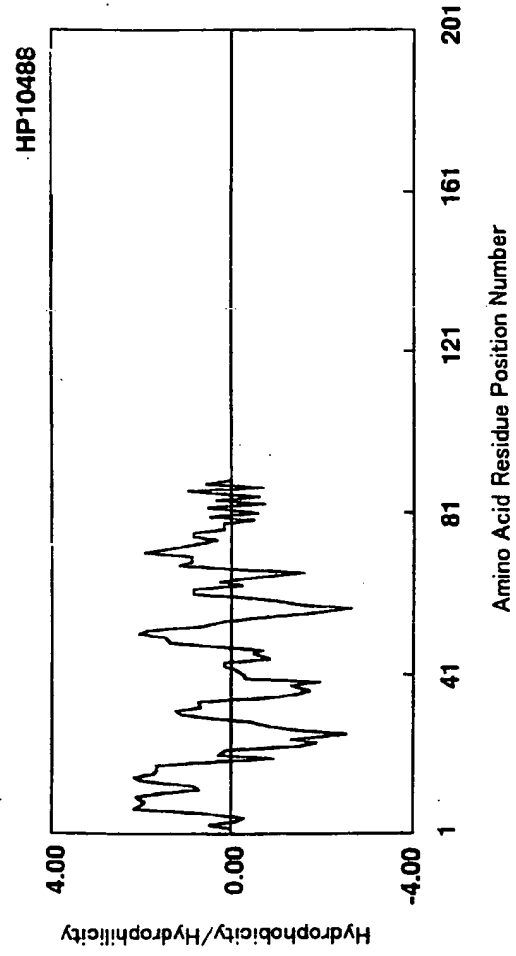


Fig.27

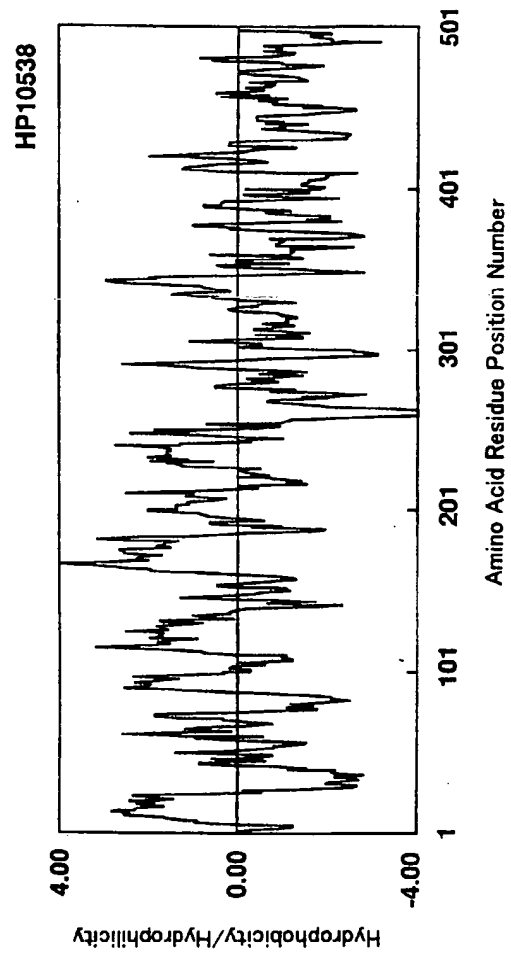


Fig. 28

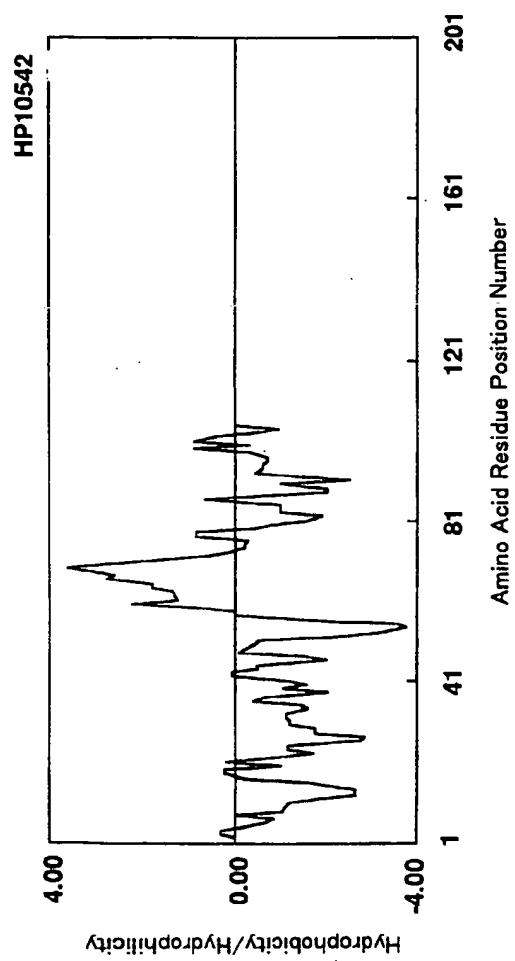


Fig. 29

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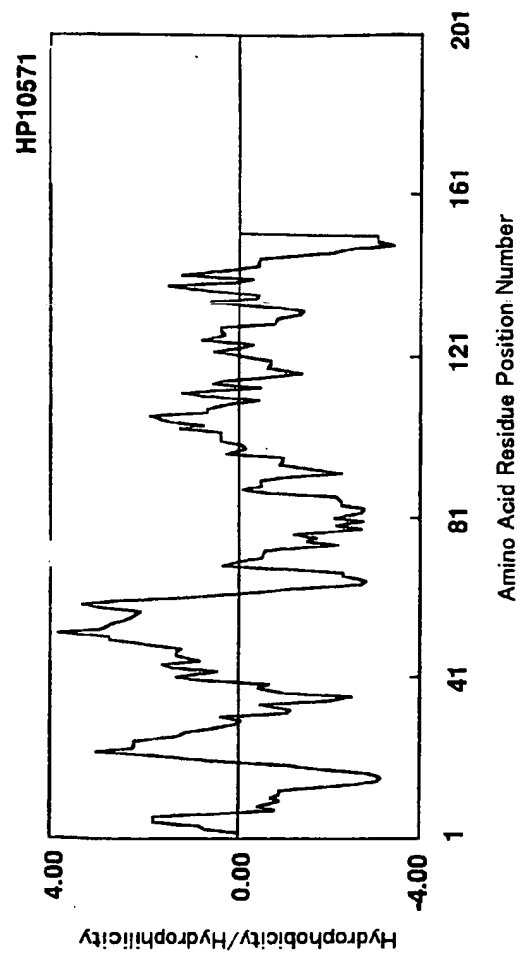


Fig. 30

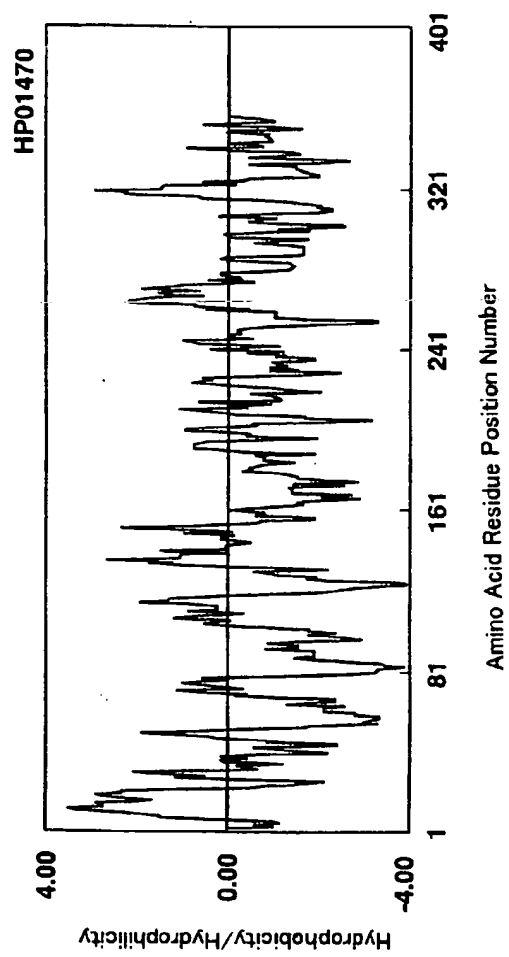


Fig. 31

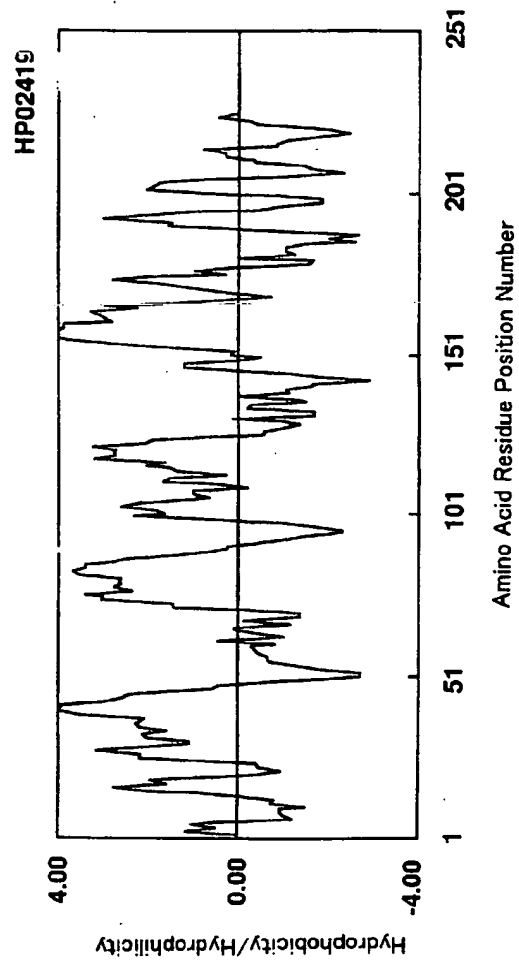


Fig.32

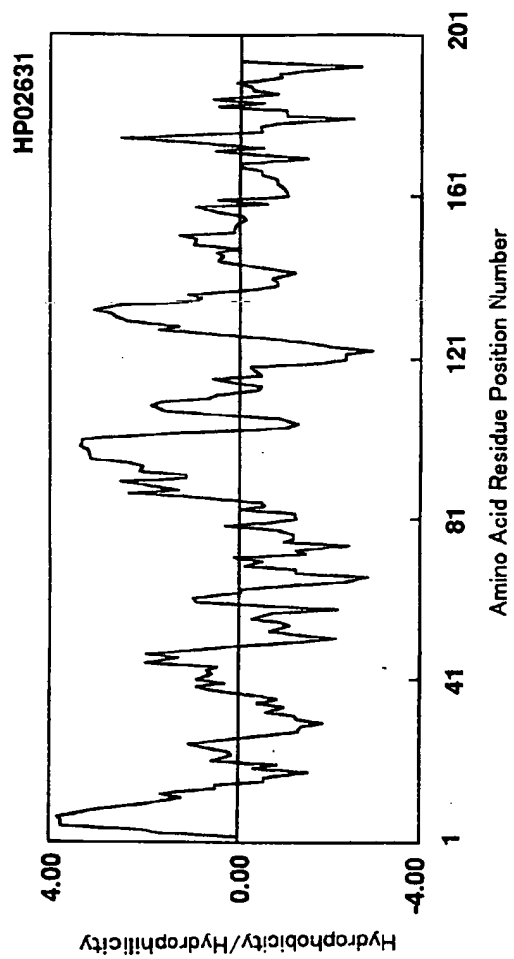


Fig. 33



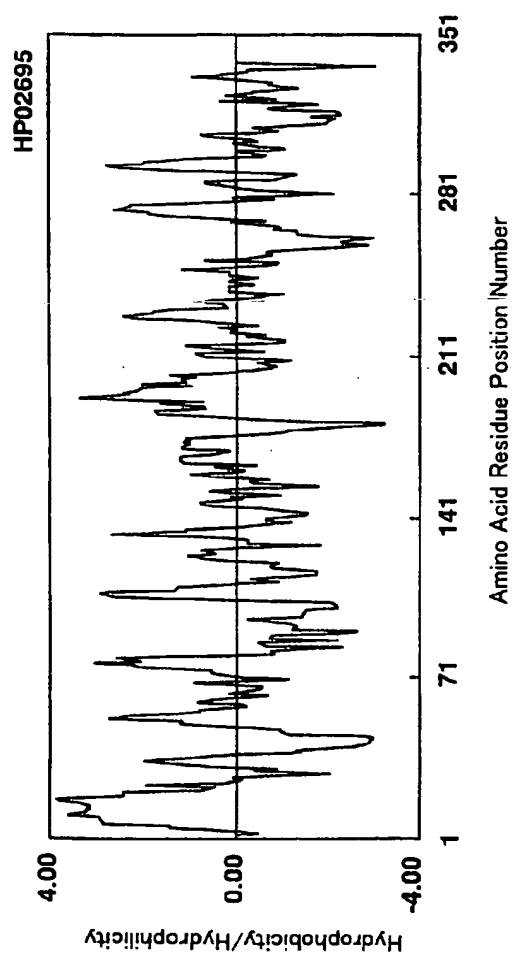


Fig. 34

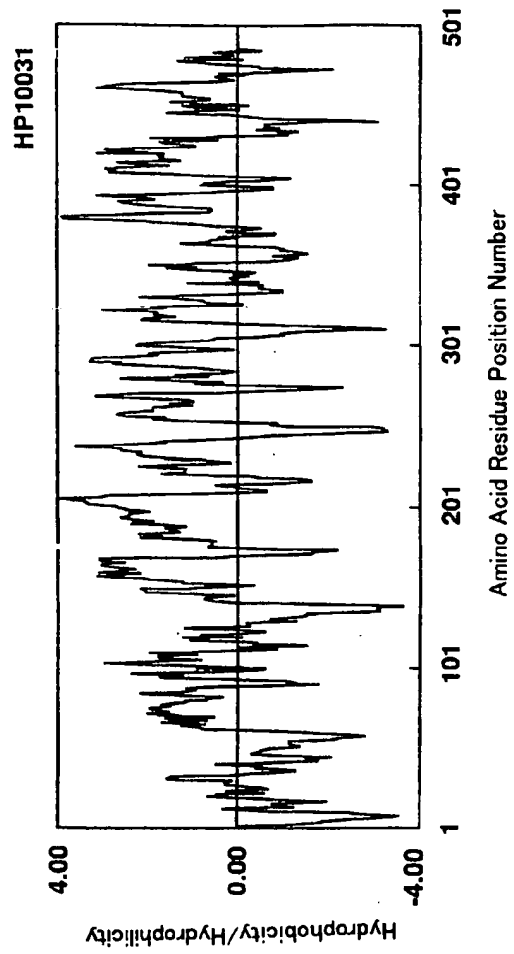


Fig. 35

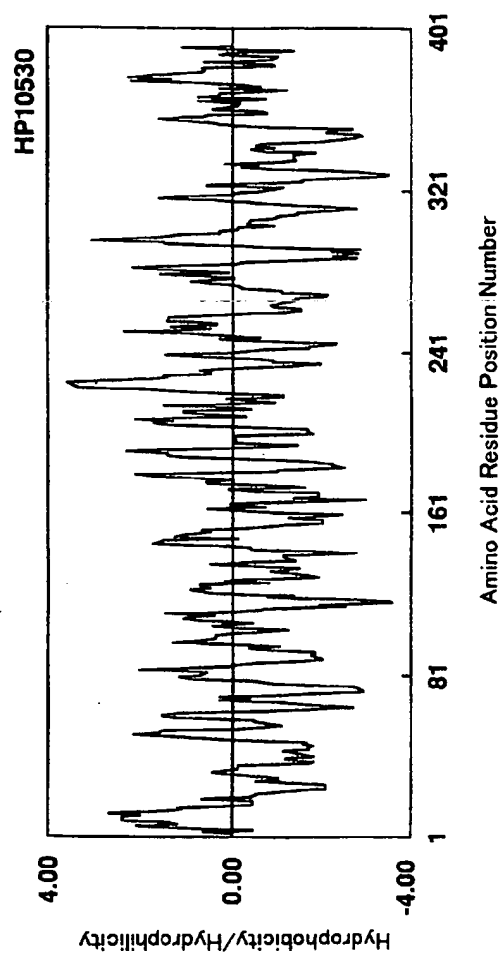


Fig. 36

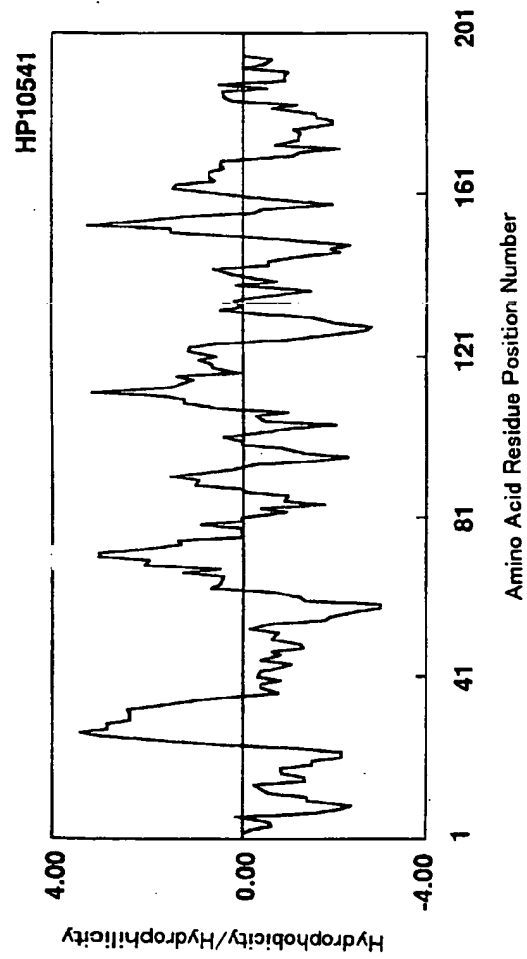


Fig.37

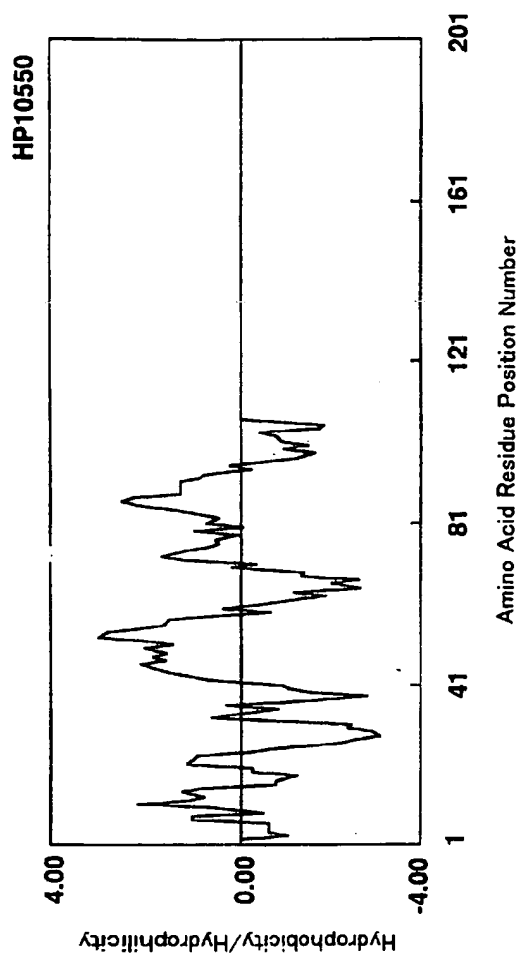


Fig. 38

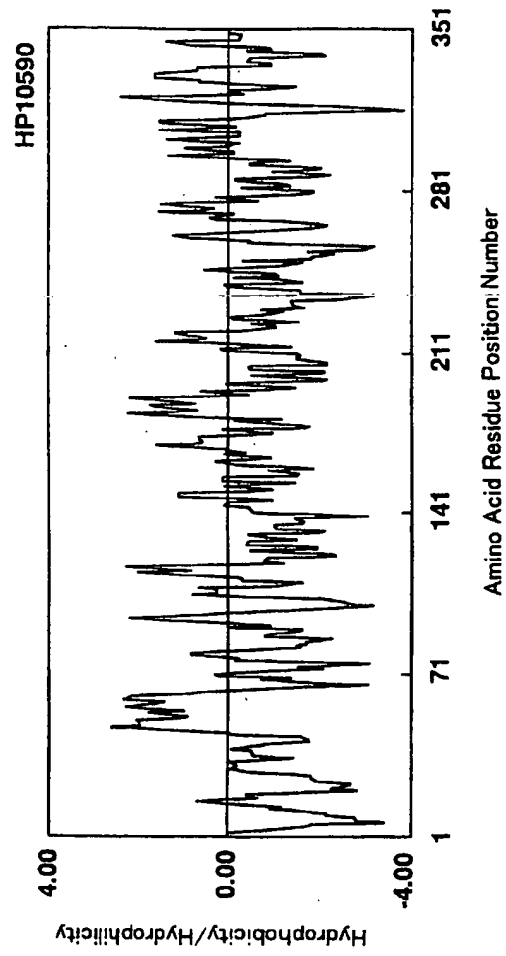


Fig. 39

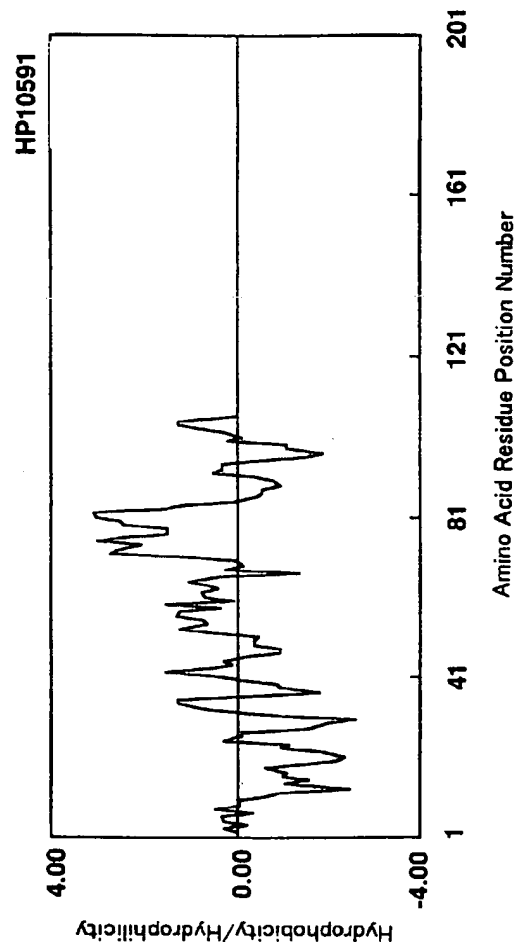


Fig. 40

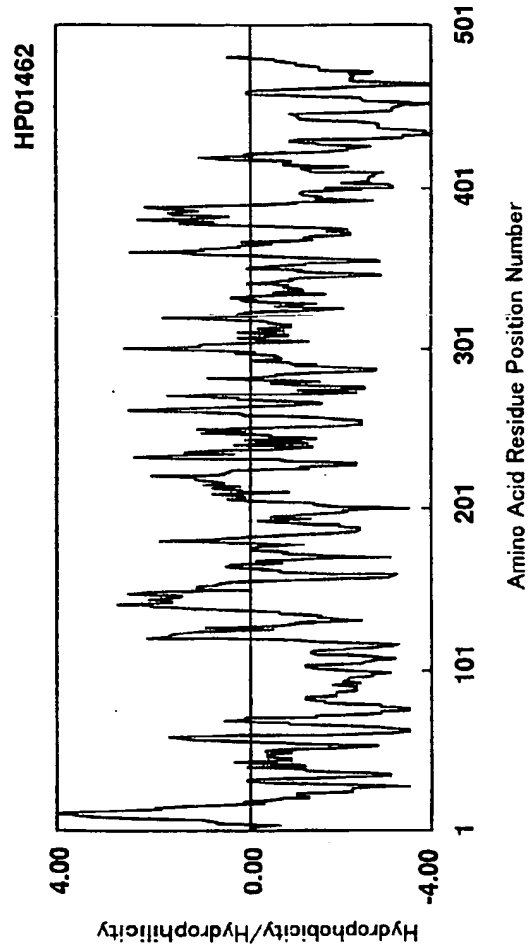


Fig. 41



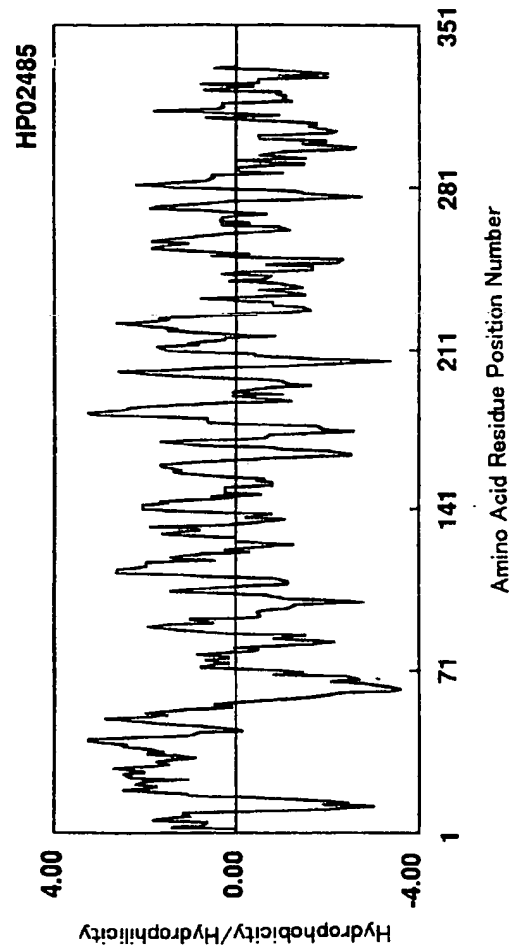


Fig.42

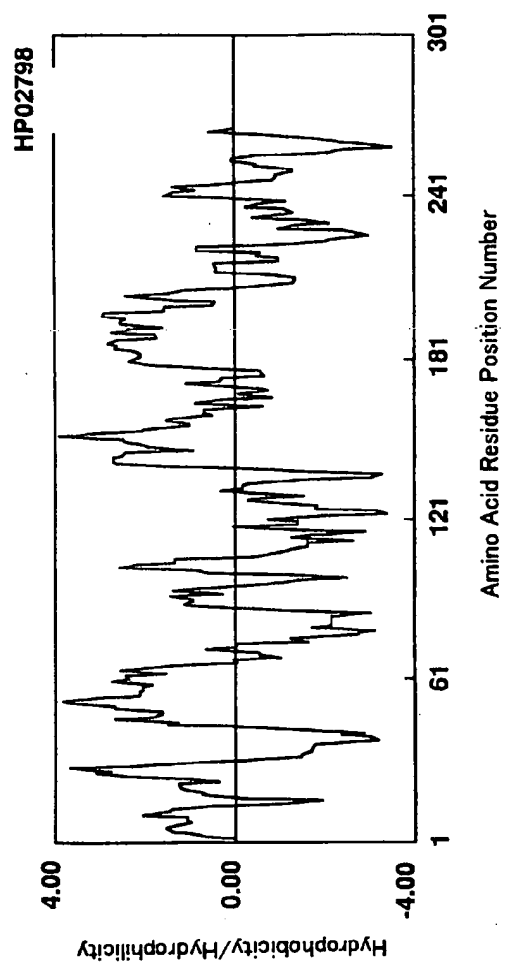


Fig. 43

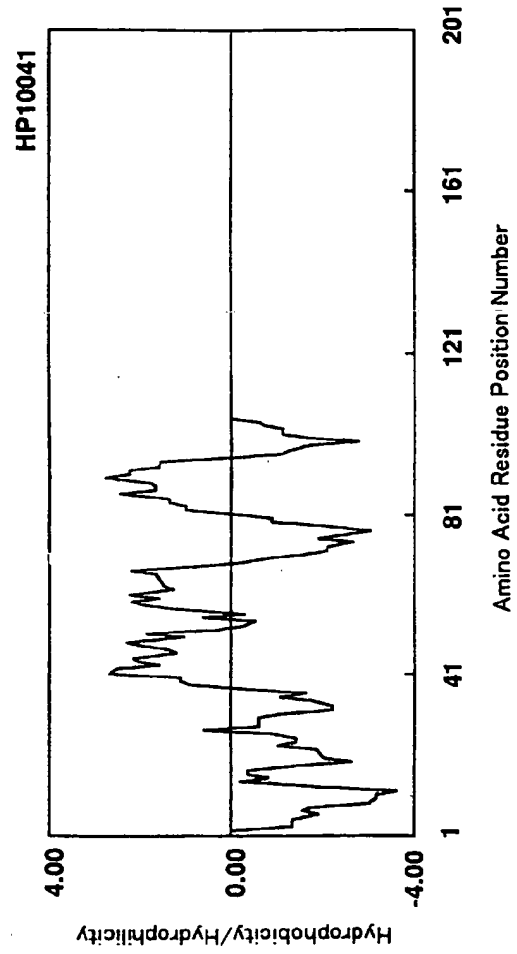


Fig. 44

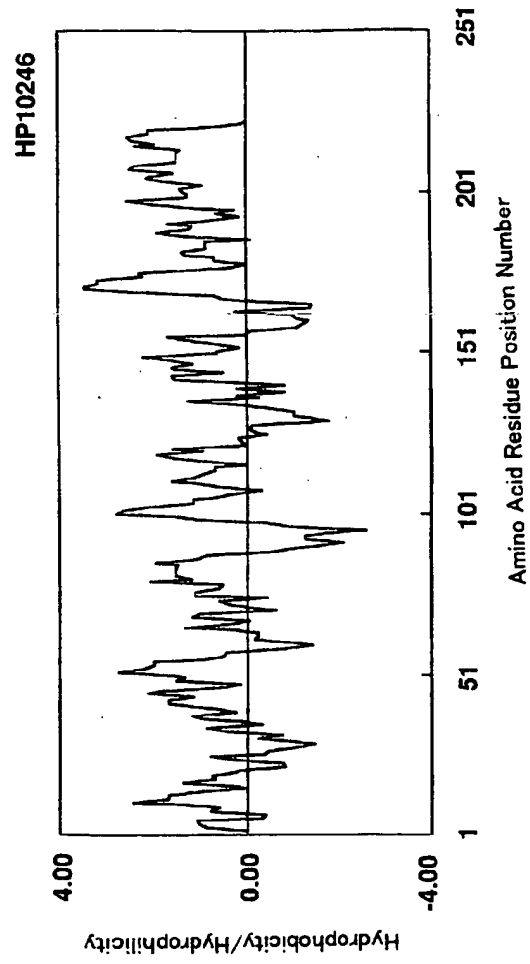


Fig. 45

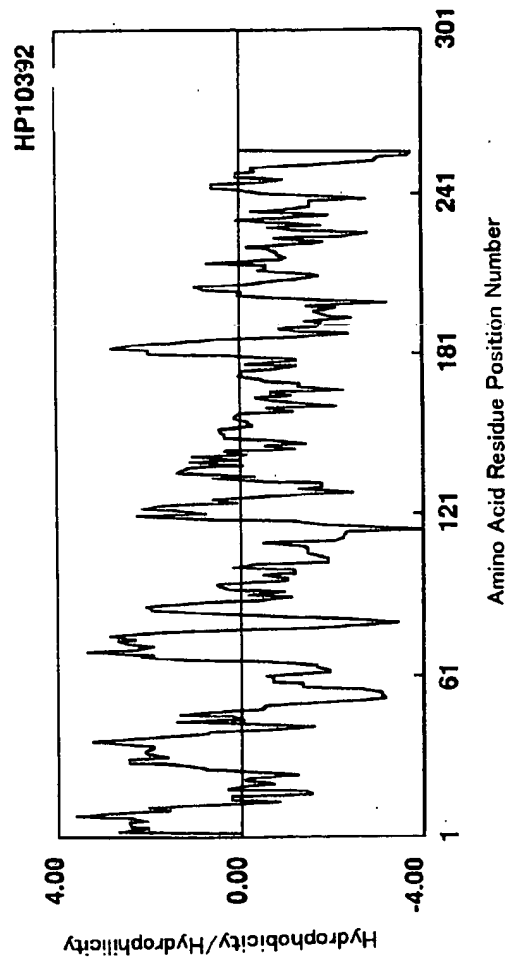


Fig. 46

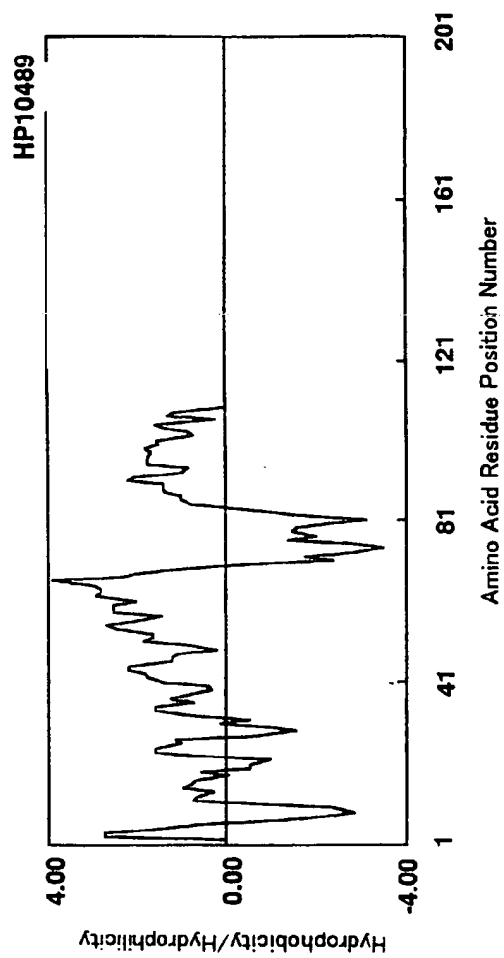


Fig.47

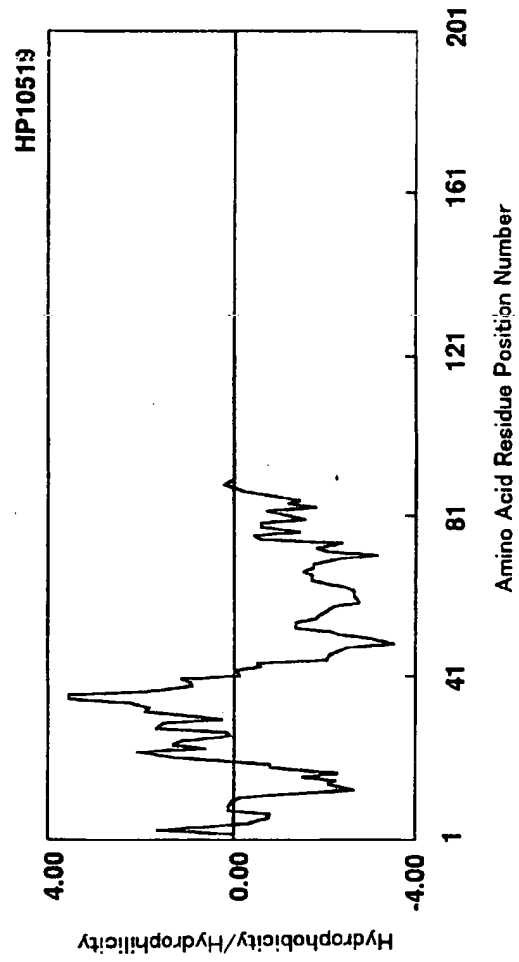


Fig. 48

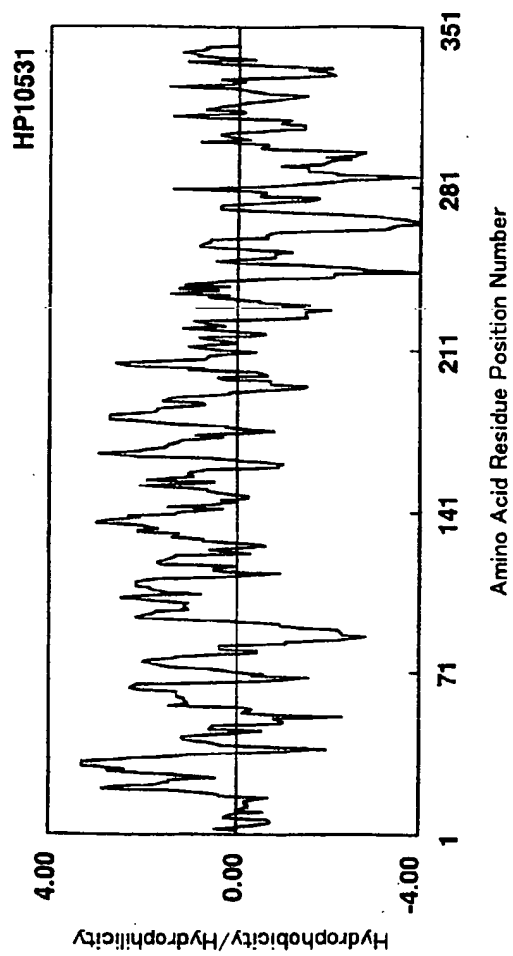


Fig. 49



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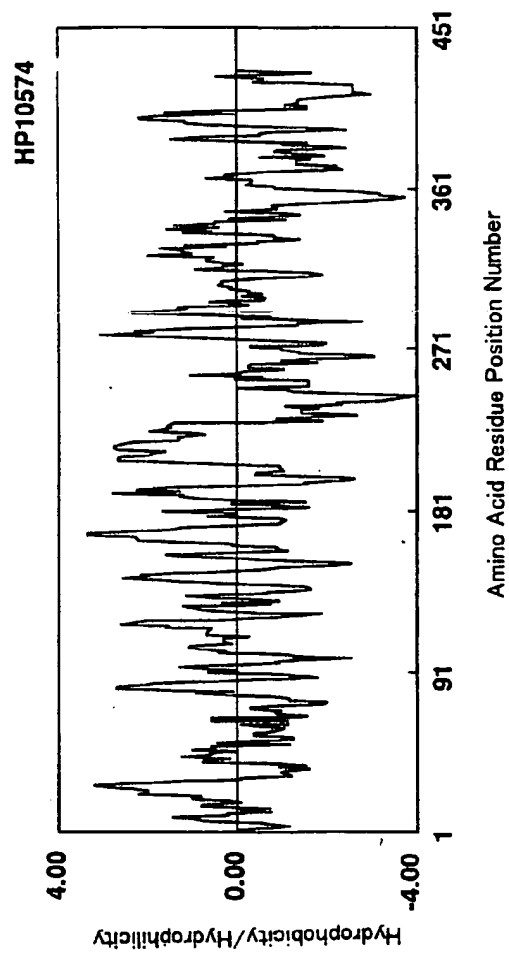


Fig. 50

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	Gly	Ala	Gln	Ile
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	Leu	Val	Leu	Gln
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	Trp	Glu	Val	Phe
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	Leu	Leu	Leu	Pro
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	Val	Asn	Leu	
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	Thr	Cys	Asp	Leu
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 10 65 70 75 80  
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accatctctg gcattataac aaagcaaat gaattattat ttcttcctgt ttatgaattt 420
gatgaagtga tgtttccaaa gaacgtgagg tgctctactt gtgatttaag gaaaccagct 480
cgatccaagc actgcagtgt gtgtaactgg tgtgtgcacc gtttcgacca tcaactgtgtt 540
tgggtgaaca actgcctcgg ggctcggacc atcaggtaact tctcatctta cgtcttgacc 600
5 ttgacggcct cggctgcacc cgtcgccatt gtgagcacea cttttctggg ccacttggtg 660
gtgatgtcag atttatacca ggagacttac atcgatgacc ttggacacct ccactgttatg 720
gacacggctt ttcttattca gtacctgttc ctgacttttc caccgattgt ctteatgttg 780
ggctttgtcg tggttctgag ctctctctcg ggtggctacc tgttgtttgt cctgtatctg 840
ggggccacca accagactac taacgagtgg tacagagggtg actgggctcg gtgccagcgt 900
10 tgtcccttg tggcctggcc tccgtcagca gagccccaag tccaccgaa cattactcc 960
catgggcttc ggagcaacct tcaagagatc tttctacctg cctttccatg tcatgagagg 1020
aagaaacagg aa 1032

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15 <211> 291
    <212> DNA
    <213> Homo sapiens

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20 atgactaaaa agaagcggga gaatctgggc gtcgctctag agatcgatgg gctagaggag 60
    aagctgtccc agtgtcggag agacctggag gccgtgaact ccagactcca cagccgggag 120
    ctgagcccag agggcaggag gtcctcggag aaggagaaaa acagcctaatt gaacaaagcc 180
    tccaaactacg agaagggaact gaagtctctt cggcaagaga accggaagaa catgctgctc 240
    tctgtggcca tctttatctt cctgacgctc gtctatgcct actggaccat g 291

```

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25 <210> 19
    <211> 372
    <212> DNA
    <213> Homo sapiens

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30 <400> 19
    atggctacgt cctcgatgtc taagggttgc tttgttttta agccaaactc caaaaagaga 60
    aagatctctc tgccaataga ggactatttt aacaaaggga aaaatgagcc tgaggacagt 120
    aagcttcgat tcgaaactta tcagttgata tggcagcaga tgaatctga aaatgagcga 180
35 ctacaagagg aattaaataa aaacttgttt gacaatctga ttgaatttct gcaaaaatca 240

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	cattctggat tccagaagaa ttcaagagac ttggggcggc aaataaaact cagagaaatt	300
	ccaaactgctg ctcttggttct tggatatat gcgtatgctt gttcatgcat gcctctctgt	360
	gtatttcggtt tt	372
5	<210> 20	
	<211> 981	
	<212> DNA	
	<213> Homo sapiens	
10	<400> 20	
	atggccgagc tcccgggggc cttctctctg gggggccctg taggcttctt gtgcctgagt	60
	gggctggcgg tggaggtgaa ggtaccacaa gaggccgctga gcaagccctt ggggaagaca	120
	gccgagctga cctgcaccta cagcacgtcg gtgggagaca gcttcgccct ggagtgagc	180
	tttgtgcagc ctgggaaacc catctctgag tcccatccaa toctgtactt caccaatggc	240
15	catctgtatc caactggctt taagtcaaaag cgggtcagcc tgcctcagaa cccccccaca	300
	gtgggggtgg ccacactgaa actgactgac gtccacccct cagatactgg aacctactc	360
	tgcacaagca acaacccacc agattttctac accaatgggt tggggotaat caaccttact	420
	gtgctggctt cccccagtaa tcccttatgc agtcagagtg gacaacccct tgtgggagc	480
	tctactgcac tgagatgcag ctcttccgag ggggctccta agccagtgtc caactgggtg	540
20	cgtcttgaa ctttctctac acctctctct ggcagcatgg ttcaagatga ggtgtctggc	600
	cagctcattc tcaccaacct ctccctgacc tctcgggca cctaccgctg tgtggccacc	660
	aaccagatgg gcagtgcatc ctgtgagctg acctctctg tgaccgaacc ctcccaagc	720
	cagtgggcgg gagctctgat tgggtgctc ctgggcgtgc tgttgctgct agttgctgct	780
	ttctgctctg tcaggttcca gaaagagagg gggagaagc ccaaggagac atatgggggt	840
25	agtgccttc gggaggatgc catcgctctt gggatctctg agcacacttg tatgagggct	900
	gattctagca aggggttctt ggaaagaccc tegtctgcca gcaccgtgac gaccaccaag	960
	tccaagctcc ctatggtcgt g	981
	<210> 21	
30	<211> 510	
	<212> DNA	
	<213> Homo sapiens	
	<220>	
	<221> CDS	
35	<222> (66)...(443)	



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<400> 21  
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 ctgcc atg gcc aag tac ctg gcc cag atc att gtg atg gcc gtg cag gtg 110  
 5 Met Ala Lys Tyr Leu Ala Gln Ile Ile Val Met Gly Val Gln Val  
 1 5 10 15  
 gtg gcc agg gcc ttt gca cgg gcc ttg cgg cag gag ttt gca gcc agc 158  
 Val Gly Arg Ala Phe Ala Arg Ala Leu Arg Gln Glu Phe Ala Ala Ser  
 20 25 30  
 10 cgg gcc gca gct gat gcc cga gga cgc gct gga cac cgg tct gca gcc 206  
 Arg Ala Ala Ala Asp Ala Arg Gly Arg Ala Gly His Arg Ser Ala Ala  
 35 40 45  
 got tcc aac ctc tcc gcc ctc agc ctc cag gag gca cag cag att ctc 254  
 Ala Ser Asn Leu Ser Gly Leu Ser Leu Gln Glu Ala Gln Gln Ile Leu  
 15 50 55 60  
 aac gtg tcc aag ctg agc cct gag gag gtc cag aag aac tat gaa cac 302  
 Asn Val Ser Lys Leu Ser Pro Glu Glu Val Gln Lys Asn Tyr Glu His  
 65 70 75  
 tta ttt aag gtg aat gat aaa tcc gtg ggt gcc tcc ttc tac ctg cag 350  
 20 Leu Phe Lys Val Asn Asp Lys Ser Val Gly Gly Ser Phe Tyr Leu Gln  
 80 85 90 95  
 tca aag gtg gtc cgc gca aag gag cgc ctg gat gag gaa ctc aaa atc 398  
 Ser Lys Val Val Arg Ala Lys Glu Arg Leu Asp Glu Glu Leu Lys Ile  
 100 105 110  
 25 cag gcc cag gag gac aga gaa aaa ggg cag atg ccc cat acg tgactgtc 450  
 Gln Ala Gln Glu Asp Arg Glu Lys Gly Gln Met Pro His Thr  
 115 120 125  
 gctcccccgc cccacccgc cgcctctaat ttatagcttg gtaataaatt tctttctgc 510  
 30 <210> 22  
 <211> 697  
 <212> DNA  
 <213> Homo sapiens  
 <220>  
 35 <221> CDS

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&lt;222&gt; (104)...(499)

&lt;400&gt; 22

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 5 cgccgcccgc tcgggtcgtg gagccaggag cgacgtcacc gcc atg gca ggc atc 115  
 Met Ala Gly Ile  
 1  
 aaa gct ttg att agt ttg tcc ttt gga gga gca atc gga ctg atg ttt 163  
 Lys Ala Leu Ile Ser Leu Ser Phe Gly Gly Ala Ile Gly Leu Met Phe  
 10 5 10 15 20  
 ttg atg ctt gga tgt gcc ctt cca ata tac aac aaa tac tgg ccc cto 211  
 Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys Tyr Trp Pro Leu  
 25 30 35  
 ttt gtt cta ttt ttt tac atc ctt tca cct att cca tac tgc ata gca 259  
 15 Phe Val Leu Phe Phe Tyr Ile Leu Ser Pro Ile Pro Tyr Cys Ile Ala  
 40 45 50  
 aga aga tta gtg gat gat aca gat gct atg agt aac gct tgt aag gaa 307  
 Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn Ala Cys Lys Glu  
 55 60 65  
 20 ctt gcc atc ttt ctt aca acg ggc att gtc gtg tca gct ttt gga ctc 355  
 Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser Ala Phe Gly Leu  
 70 75 80  
 cct att gta ttt gcc aga gca cat ctg att gag tgg gga gct tgt gca 403  
 Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp Gly Ala Cys Ala  
 25 85 90 95 100  
 ctt gtt ctc aca gga aac aca gtc atc ttt gca act ata cta ggc ttt 451  
 Leu Val Leu Thr Gly Asn Thr Val Ile Phe Ala Thr Ile Leu Gly Phe  
 105 110 115  
 ttc ttg gtc ttt gga agc aat gac gac ttc agc tgg cag cag tgg tgaa 500  
 30 Phe Leu Val Phe Gly Ser Asn Asp Asp Phe Ser Trp Gln Gln Trp  
 120 125 130  
 aagaaattac tgaactattg tcaaatggac ttcctgtcat ttgttgcca ttcacgcaca 560  
 caggagatgg ggcagttaat gctgaatggt atagcaagcc tcttgggggt attttagggtg 620  
 ctcccttctc acttttattg taagcatact attttcacag agacttgctg aaggattaaa 680  
 35 aggattttct cttttgg 697

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5  <213> Homo sapiens
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gtgacacagc ggcaggcgtt agggctcggg agccgcgagc ctggcctcgt cctagagetc 180
ggccgagccg tcgccgccgt cgtcccccgc ccccgatcag caaacccgcg ccgcgggcgc 240
15 gcccccgctc tgcgctgtct ctccgatggc gtcgcctca ggggcc atg gcg aag 295
Met Ala Lys
1
cac gag cag atc ctg gtc ctc gat ccg ccc aca gac ctc aaa ttc aaa 343
His Glu Gln Ile Leu Val Leu Asp Pro Pro Thr Asp Leu Lys Phe Lys
20 5 10 15
ggc ccc ttc aca gat gta gtc act aca aat ctt aaa ttg cga aat cca 391
Gly Pro Phe Thr Asp Val Val Thr Thr Asn Leu Lys Leu Arg Asn Pro
20 25 30 35
tcg gat aga aaa gtg tgt ttc aaa gtg aag act aca gca cct cgc cgg 439
25 Ser Asp Arg Lys Val Cys Phe Lys Val Lys Thr Thr Ala Pro Arg Arg
40 45 50
tac tgt gtg agg ccc aac agt gga att att gac cca ggg tca act gtg 487
Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Pro Gly Ser Thr Val
55 60 65
30 act gtt tca gta atg cta cag ccc ttt gac tat gat ccg aat gaa aag 535
Thr Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro Asn Glu Lys
70 75 80
agt aaa cac aag ttt atg gta cag aca att ttt gct cca cca aac act 583
35 Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro Pro Asn Thr
85 90 95

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	tca gat atg gaa gct gtg tgg aaa gag gca aaa cct gat gaa tta atg	631
	Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Asp Glu Leu Met	
	100 105 110 115	
	gat tcc aaa ttg aga tgc gta ttt gaa atg ccc aat gaa aat gat aaa	679
5	Asp Ser Lys Leu Arg Cys Val Phe Glu Met Pro Asn Glu Asn Asp Lys	
	120 125 130	
	ttg aat gat atg gaa cct agc aaa gct gtt cca ctg aat gca tct aag	727
	Leu Asn Asp Met Glu Pro Ser Lys Ala Val Pro Leu Asn Ala Ser Lys	
	135 140 145	
10	caa gat gga cct atg cca aaa cca cac agt gtt tca ctt aat gat acc	775
	Gln Asp Gly Pro Met Pro Lys Pro His Ser Val Ser Leu Asn Asp Thr	
	150 155 160	
	gaa aca agg aaa cta atg gaa gag tgt aaa aga ctt cag gga gaa atg	823
	Glu Thr Arg Lys Leu Met Glu Glu Cys Lys Arg Leu Gln Gly Glu Met	
15	165 170 175	
	atg aag cta tca gaa gaa aat cgg cac ctg aga gat gaa ggt tta agg	871
	Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu Gly Leu Arg	
	180 185 190 195	
	ctc aga aag gta gca cat tgc gat aaa oct gga tca acc tca act gca	919
20	Leu Arg Lys Val Ala His Ser Asp Lys Pro Gly Ser Thr Ser Thr Ala	
	200 205 210	
	tcc ttc aga gat aat gtc acc agt cct ctt cct tca ctt ctt gtt gta	967
	Ser Phe Arg Asp Asn Val Thr Ser Pro Leu Pro Ser Leu Leu Val Val	
	215 220 225	
25	att gca gcc att ttc att gga ttc ttt cta ggg aaa ttc atc ttg	1012
	Ile Ala Ala Ile Phe Ile Gly Phe Phe Leu Gly Lys Phe Ile Leu	
	230 235 240	
	tagagtgaag catgcagagt gctgtttctt tttttttttt ttctcttgac cagaaaaa	1070
	gatttggtta cctaccattt cattggtagt atggcccacg gtgaccattt tttgtgtgt	1130
30	acagcgtcat ataggettgt cctttaatga tctcttacgg tttagaaaca caataaaaac	1190
	aaactgttcg gctactggac aggttgtata ttaccagatc atcactagca gatgtcagtt	1250
	gcacattgag tcttttatga aattcataaa taaagaattg ttctttcttt gtgggtttta	1310
	taagagttca agaattgttc agagtcttgt aaatgttatt ttaataatcc ctttaaattt	1370
	tatctgttgc tgttacctct tgaaatatga tttatttaga ttgctaatac cactcattca	1430
35	ggaaatgcca agaggtattc cttggggaaa tgggtcctct tacagtgtaa atttttctc	1490

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ctttaccttt gctaataatca tggcagaatt tttcttatec cttgtgagge agttgttgac 1550
tgagtttttc atccttacaa tctgttccca tggatatttaa cataaaaaaa aataaaactg 1610
ttaacagat 1619

5 <210> 24
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  <213> Homo sapiens
  <220>
10 <221> CDS
  <222> (65)...(859)

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15 gacc atg ttc gtt ccc tgc ggg gag tgc gcc ccc gac ctt gcc ggc ttc 109
    Met Phe Val Pro Cys Gly Glu Ser Ala Pro Asp Leu Ala Gly Phe
      1         5         10        15
acc ctc cta atg cca gca gta tct gtt gga aat gtt gcc cag ctt gca 157
Thr Leu Leu Met Pro Ala Val Ser Val Gly Asn Val Gly Gln Leu Ala
20          20          25          30
atg gat ctg att att tct aca ctg aat atg tct aag att ggt tac ttc 205
Met Asp Leu Ile Ile Ser Thr Leu Asn Met Ser Lys Ile Gly Tyr Phe
      35          40          45
tat acc gat tgt ctt gtg cca atg gtt gga aac aat cca tat gcg acc 253
25 Tyr Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr
      50          55          60
aca gaa gga aat tca aca gaa ctt agc ata aat gct gaa gtg tat tca 301
Thr Glu Gly Asn Ser Thr Glu Leu Ser Ile Asn Ala Glu Val Tyr Ser
      65          70          75
ttg cct tca aga aag ctg gtg gct cta cag tta aga tcc att ttt att 349
30 Leu Pro Ser Arg Lys Leu Val Ala Leu Gln Leu Arg Ser Ile Phe Ile
      80          85          90          95
aag tat aaa tca aag cca ttc tgt gaa aaa ctg ctt tcc tgg gtg aaa 397
Lys Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys
35          100          105          110

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	agc agt ggc tgt gcc aga gtc att gtt ctt tcg agc agt cat tca tat	445
	Ser Ser Gly Cys Ala Arg Val Ile Val Leu Ser Ser Ser His Ser Tyr	
	115 120 125	
	cag cgt aat gat ctg cag ctt cgt agt act ccc ttc cgg tac cta ctt	493
5	Gln Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu	
	130 135 140	
	aca cct tcc atg caa aaa agt gtt caa aat aaa ata aag agc ctt aac	541
	Thr Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn	
	145 150 155	
10	tggt gaa gaa atg gaa aaa agc cgg tgc att cct gaa ata gat gat tcc	589
	Trp Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser	
	160 165 170 175	
	gag ttt tgt atc cgc att cgg gga gga ggt atc aca aaa aca ctc tat	637
	Glu Phe Cys Ile Arg Ile Pro Gly Gly Gly Ile Thr Lys Thr Leu Tyr	
15	180 185 190	
	gat gaa agc tgt tct aaa gaa atc caa atg gca gtt ctg ctg aaa ttt	685
	Asp Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe	
	195 200 205	
	gtt tca gaa ggg gac aac atc cca gat gca tta ggt ctt gtt gag tat	733
20	Val Ser Glu Gly Asp Asn Ile Pro Asp Ala Leu Gly Leu Val Glu Tyr	
	210 215 220	
	ctt aat gag tgg ctt cag ata ctc aaa cca ctt agc gat gac ccc aca	781
	Leu Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr	
	225 230 235	
25	gta tct gcc tca cgg tgg aaa ata cca agt tct tgg aga tta ctc ttt	829
	Val Ser Ala Ser Arg Trp Lys Ile Pro Ser Ser Trp Arg Leu Leu Phe	
	240 245 250 255	
	ggc agt ggt ctt ccc cct gca ctt ttc tgatctaatt tctgttttat acct	880
	Gly Ser Gly Leu Pro Pro Ala Leu Phe	
30	260	
	tatacccaaa acacttacta ccaacacagc tgtaaacat totatacaaa aaaattgtat	940
	gatctggtat taggaatta ctttcacagt aaatatcaaa gaaaaagat taagggtctc	1000
	tttgccatgc ttttcacat atgcaccaaa tgtaaat ttt gtacaataaa attttat ttc	1060
	ctaagt	1066
35		

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<213> Homo sapiens
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<221> CDS
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	1	
	ggg tat cgg ttg tcc cag cct ttt gag tcc tat atc act gcg cct ccc	104
	Gly Ser Arg Leu Ser Gln Pro Phe Glu Ser Tyr Ile Thr Ala Pro Pro	
15	5 10 15	
	ggg acc gcc gcc gcg ccc gcc aaa cct gcg ccc cca gct aca ccc gga	152
	Gly Thr Ala Ala Ala Pro Ala Lys Pro Ala Pro Pro Ala Thr Pro Gly	
	20 25 30	
	gcg ccg acc tcc cca gca gaa cac cgc ctg ttg aag acc tgc tgg agc	200
20	Ala Pro Thr Ser Pro Ala Glu His Arg Leu Leu Lys Thr Cys Trp Ser	
	35 40 45	
	tgt cgc gtg ctt tct ggg ttg ggg ctg atg ggg gcg gcc ggg tac gtg	248
	Cys Arg Val Leu Ser Gly Leu Gly Leu Met Gly Ala Gly Gly Tyr Val	
	50 55 60 65	
25	tac tgg gtg gca cgg aag ccc atg aag atg gga tac ccc ccg agt cca	296
	Tyr Trp Val Ala Arg Lys Pro Met Lys Met Gly Tyr Pro Pro Ser Pro	
	70 75 80	
	tgg acc att acg cag atg gtc atc gcc ctg agc att gcc acc tgg ggt	344
	Trp Thr Ile Thr Gln Met Val Ile Gly Leu Ser Ile Ala Thr Trp Gly	
30	85 90 95	
	atc gtt gtc atg gca gac ccc aaa ggg aag gcc tac cgc gtt gtt t	390
	Ile Val Val Met Ala Asp Pro Lys Gly Lys Ala Tyr Arg Val Val	
	100 105 110	
	gaaagtacca coagtgaaatc tctctctgt cctctgccct ttcccgtga cacacacagc	450
35	aggcatggaa ttttaatgggt gttctggaca gacacttgta catggacaga catcaactact	510

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gtggatacta caagaactgag aagaaaatcg tatgttgta ttctetgggt atggagtgtt 570
tgtggccttc acagatttca caggaacca taaatccctc agagaagt 618

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  <212> DNA
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  <220>
  <221> CDS
10 <222> (413)...(853)

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15 ggtgagcggg cgctagggcc gcgagccccc gccggccctt cctccagcgc cctgcggacc 180
ccgcagaagg cgctcgcctc cctagccccc aaaaacatat cgatttttct cgctgtggca 240
acggggacgt cctgatagat cctctgctcc aataggcaac tccggccttc cctgccctga 300
cctggaacct ctgggagggc tgcagagtaa gtccgcctc tgcgtccga cggaggcacc 360
aggcctgtgg agtaggtccc tctgttccga caggtgcgac acttggeget cc atg ctt 418
20 Met Leu
      1
gcg ggt gcc ggg agg cct ggc ctc ccc cag ggc cgc cac ctc tgc tgg 466
Ala Gly Ala Gly Arg Pro Gly Leu Pro Gln Gly Arg His Leu Cys Trp
      5      10      15
25 ttg ctc tgt gct ttc acc tta aag ctc tgc caa gca gag gct ccc gtg 514
Leu Leu Cys Ala Phe Thr Leu Lys Leu Cys Gln Ala Glu Ala Pro Val
      20      25      30
cag gaa gag aag ctg tca gca agc acc tca aat ttg cca tgc tgg ctg 562
Gln Glu Glu Lys Leu Ser Ala Ser Thr Ser Asn Leu Pro Cys Trp Leu
30 35      40      45      50
gtg gaa gag ttt gtg gta gca gaa gag tgc tct cca tgc tct aat ttc 610
Val Glu Glu Phe Val Val Ala Glu Glu Cys Ser Pro Cys Ser Asn Phe
      55      60      65
cgg gct aaa act acc cct gag tgt ggt ccc aca gga tat gta gag aaa 658
35 Arg Ala Lys Thr Thr Pro Glu Cys Gly Pro Thr Gly Tyr Val Glu Lys

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	70	75	80	
	atc aca tgc agc tca tct aag aga aat gag ttc aaa agc tgc cgc tca			706
	Ile Thr Cys Ser Ser Ser Lys Arg Asn Glu Phe Lys Ser Cys Arg Ser			
	85	90	95	
5	gct ttg atg gaa caa cgc tta ttt tgg aag ttc gaa ggg gct gtc gtg			754
	Ala Leu Met Glu Gln Arg Leu Phe Trp Lys Phe Glu Gly Ala Val Val			
	100	105	110	
	tgt gtg gcc ctg atc ttc gct tgt ctt gtc atc att cgt cag cga caa			802
	Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Ile Arg Gln Arg Gln			
10	115	120	125	130
	ttg gac aga aag gct ctg gaa aag gtc cgg aag caa atc gag tcc ata			850
	Leu Asp Arg Lys Ala Leu Glu Lys Val Arg Lys Gln Ile Glu Ser Ile			
	135	140	145	
	tagctacatt ccacccttgt atcctgggtc ttgagaccc tatctcagac agtgaagtg			910
15	aaatggactg atttgactc ttggttcttt ggagccttgt ggtggaatcc cctttccccc			970
	atctctctct ttcagatcat taatgagcag aataaaaaga gtaaatggt t			1021
	<210> 27			
	<211> 1432			
20	<212> DNA			
	<213> Homo sapiens			
	<220>			
	<221> CDS			
	<222> (331)...(1365)			
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	gcccagctcc ggggcccgc cgggtgcccc tccgagcctg ctgcactcca cgtccccta			120
	ccagggtccc agccccagg gaaatctccg accaggcccc cccaggagcc agatccaggc			180
30	tcctggaaga accatgtccg gcagctactg gtcattgccag gcacacactg ctgcccaga			240
	ggagctgtg tttgaattat ctgtgaatgt tgggaagagg aatgccagag ctgcggctg			300
	aaaattaccc aaccaagaga aatctgcagg atg gac ttt ctg gtc etc ttc ttg			354
		Met Asp Phe Leu Val Leu Phe Leu		
		1	5	
35	ttc tac ctg gct tcc gtg ctg atg ggt ctt gtt ctt atc tgc gtc tgc			402

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	Phe Tyr Leu Ala Ser Val Leu Met Gly Leu Val Leu Ile Cys Val Cys	
	10 15 20	
	tcg aaa acc cat agc ttg aaa ggc ctg gcc agg gga gga gca cag ata	450
	Ser Lys Thr His Ser Leu Lys Gly Leu Ala Arg Gly Gly Ala Gln Ile	
5	25 30 35 40	
	ttt tcc tgt ata att cca gaa tgt ctt cag aga gcc gtg cat gga ttg	498
	Phe Ser Cys Ile Ile Pro Glu Cys Leu Gln Arg Ala Val His Gly Leu	
	45 50 55	
	ctt cat tac ctt ttc cat acg aga aac cac acc ttc att gtc ctg cac	546
10	Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe Ile Val Leu His	
	60 65 70	
	ctg gtc ttg cca ggg atg gtt tat act gag tac acc tgg gaa gta ttt	594
	Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr Trp Glu Val Phe	
	75 80 85	
15	ggc tac tgt cag gag ctg gag ttg tcc ttg cat tac ctt ctt ctg ccc	642
	Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr Leu Leu Leu Pro	
	90 95 100	
	tat ctg ctg cta ggt gta aac ctg ttt ttt ttc acc ctg act tgt gga	690
	Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Phe Thr Leu Thr Cys Gly	
20	105 110 115 120	
	acc aat cct ggc att ata aca aaa gca aat gaa tta tta ttt ctt cat	738
	Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu Leu Phe Leu His	
	125 130 135	
	gtt tat gaa ttt gat gaa gtg atg ttt cca aag aac gtg agg tgc tct	786
25	Val Tyr Glu Phe Asp Glu Val Met Phe Pro Lys Asn Val Arg Cys Ser	
	140 145 150	
	act tgt gat tta agg aaa cca gct cga tcc aag cac tgc agt gtg tgt	834
	Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Lys His Cys Ser Val Cys	
	155 160 165	
30	aac tgg tgt gtg cac cgt ttc gac cat cac tgt gtt tgg gtg aac aac	882
	Asn Trp Cys Val His Arg Phe Asp His His Cys Val Trp Val Asn Asn	
	170 175 180	
	tgc atc ggg gcc tgg aac atc agg tac ttc ctc atc tac gtc ttg acc	930
	Cys Ile Gly Ala Trp Asn Ile Arg Tyr Phe Leu Ile Tyr Val Leu Thr	
35	185 190 195 200	

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	ttg acg gcc tag gct gcc acc gtc gcc att gtg agc acc act ttt ctg	978
	Leu Thr Ala Ser Ala Ala Thr Val Ala Ile Val Ser Thr Thr Phe Leu	
	205 210 215	
	gtc cac ttg gtg gtg atg tca gat tta tac cag gag act tac atc gat	1026
5	Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu Thr Tyr Ile Asp	
	220 225 230	
	gac ett gga cac ctc cat gtt atg gac acg gtc ttt ett att cag tac	1074
	Asp Leu Gly His Leu His Val Met Asp Thr Val Phe Leu Ile Gln Tyr	
	235 240 245	
10	ctg ttc ctg act ttt cca cgg att gtc ttc atg ctg ggc ttt gtc gtg	1122
	Leu Phe Leu Thr Phe Pro Arg Ile Val Phe Met Leu Gly Phe Val Val	
	250 255 260	
	GTT CTG AGC TTC CTC CTG GGT GGC TAC CTG TTG TTT GTC CTG TAT CTG	1170
	Val Leu Ser Phe Leu Leu Gly Gly Tyr Leu Leu Phe Val Leu Tyr Leu	
15	265 270 275 280	
	gcg gcc acc aac cag act act aac gag tgg tac aga ggt gac tgg gcc	1218
	Ala Ala Thr Asn Gln Thr Thr Asn Glu Trp Tyr Arg Gly Asp Trp Ala	
	285 290 295	
	tgg tgc cag cgt tgt ccc ett gtg gcc tgg cct cgg tca gca gag ccc	1266
20	Trp Cys Gln Arg Cys Pro Leu Val Ala Trp Pro Pro Ser Ala Glu Pro	
	300 305 310	
	caa gtc cac cgg aac att cac tcc cat ggg ett cgg agc aac ett caa	1314
	Gln Val His Arg Asn Ile His Ser His Gly Leu Arg Ser Asn Leu Gln	
	315 320 325	
25	gag atc ttt cta cct gcc ttt cca tgt cat gag agg aag aaa caa gaa	1362
	Glu Ile Phe Leu Pro Ala Phe Pro Cys His Glu Arg Lys Lys Gln Glu	
	330 335 340	
	tgacaagtgt atgactgcct ttgagctgta gtcccggttt atttacacat gtggatcc	1420
	tcgttttcca ag	1432
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	<211> 601	
	<212> DNA	
	<213> Homo sapiens	
35	<220>	

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&lt;221&gt; CDS

&lt;222&gt; (62)...(355)

&lt;400&gt; 28

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5  atgcgcacat agcgacttgg tgggcgcgtc cagtgatgac tgggggatcc cggaagtaa    60
   c atg act aaa aag aag cgg gag aat ctg ggc gtc gct cta gag atc gat    109
     Met Thr Lys Lys Lys Arg Glu Asn Leu Gly Val Ala Leu Glu Ile Asp
       1         5         10        15
10  ggg cta gag gag aag ctg tcc cag tgt cgg aga gac ctg gag gcc gtg    157
     Gly Leu Glu Glu Lys Leu Ser Gln Cys Arg Arg Asp Leu Glu Ala Val
       20        25        30
     aac tcc aga ctc cac agc cgg gag ctg agc cca gag gcc agg agg tcc    205
     Asn Ser Arg Leu His Ser Arg Glu Leu Ser Pro Glu Ala Arg Arg Ser
       35        40        45
15  ctg gag aag gag aaa aac agc cta atg aac aaa gcc tcc aac tac gag    253
     Leu Glu Lys Glu Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Glu
       50        55        60
     aag gaa ctg aag ttt ctt cgg caa gag aac cgg aag aac atg ctg ctc    301
     Lys Glu Leu Lys Phe Leu Arg Gln Glu Asn Arg Lys Asn Met Leu Leu
20  65         70         75         80
     tct gtg gcc atc ttt atc ctc ctg acg ctc gtc tat gcc tac tgg acc    349
     Ser Val Ala Ile Phe Ile Leu Leu Thr Leu Val Tyr Ala Tyr Trp Thr
       85        90        95
25  atg tgagcctggc acttccccac aaccagcaca ggcttccact tggccccct    400
     Met

     tgatcaggat caagcaggca cttcaagcct caataggacc aaggtgctgg ggtgtcccc    460
     tcccaacctt gtgttaagc atggcttccct ggcggccag gccttgccct cctggccctgc    520
     tgggggggtc cgggtctcca gaaggacatg gtgctggtcc ctcccttagc ccaaggggaga    580
30  ggcaataaag acacaaagct g                                601

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&lt;210&gt; 29

&lt;211&gt; 585

&lt;212&gt; DNA

35 &lt;213&gt; Homo sapiens

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&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (78)...(452)

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gcagagtoag taagacc atg gct aag tcc tcg atg tct aag ggt tgc ttt 110  
Met Ala Thr Ser Ser Met Ser Lys Gly Cys Phe  
1 5 10

10 gtt ttt aag cca aac tcc aaa aag aga aag atc tct ctg cca ata gag 158  
Val Phe Lys Pro Asn Ser Lys Lys Arg Lys Ile Ser Leu Pro Ile Glu  
15 20 25  
gac tat ttt aac aaa ggg aaa aat gag cct gag gac agt aag ctt cga 206  
Asp Tyr Phe Asn Lys Gly Lys Asn Glu Pro Glu Asp Ser Lys Leu Arg  
15 30 35 40  
ttc gaa act tat cag ttg ata tgg cag cag atg aaa tct gaa aat gag 254  
Phe Glu Thr Tyr Gln Leu Ile Trp Gln Gln Met Lys Ser Glu Asn Glu  
45 50 55  
cga cta caa gag gaa tta aat aaa aac ttg ttt gac aat ctg att gaa 302  
Arg Leu Gln Glu Glu Leu Asn Lys Asn Leu Phe Asp Asn Leu Ile Glu  
20 60 65 70 75  
ttt ctg caa aaa tca cat tct gga ttc cag aag aat tca aga gac ttg 350  
Phe Leu Gln Lys Ser His Ser Gly Phe Gln Lys Asn Ser Arg Asp Leu  
80 85 90

25 ggc ggt caa ata aaa ctc aga gaa att cca act gct gct ctt gtt ctt 398  
Gly Gly Gln Ile Lys Leu Arg Glu Ile Pro Thr Ala Ala Leu Val Leu  
95 100 105  
ggc ata tat gcg tat gtt tgt tca tgc atg cat ctc tgt gta ttt cgt 446  
Gly Ile Tyr Ala Tyr Val Cys Ser Cys Met His Leu Cys Val Phe Arg  
30 110 115 120  
ttt taaattttt tttattgttg agaatagtgg aaggaccrgt tttgatgagc c 500  
Phe

tattttgtct ctcttatttg taacaattaaa ccaactatag tttatattac atattttcaa 560  
35 aaaccaataa aaattcctta tcttt 585

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 Ala Glu Leu Pro Gly Pro Phe Leu Cys Gly Ala Leu Leu Gly Phe Leu  
 5 10 15  
 tgc ctg agt ggg ctg gcc gtg gag gtg aag gta ccc aca gag ccc ctg 155  
 Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr Glu Pro Leu  
 20 25 30  
 20 agc acg ccc ctg ggg aag aca gcc gag ctg acc tgc acc tac agc acg 203  
 Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys Thr Tyr Ser Thr  
 35 40 45  
 tcg gtg gga gac agc ttc gcc ctg gag tgg agc ttt gtg cag cct ggg 251  
 Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro Gly  
 25 50 55 60 65  
 aaa ccc atc tct gag tcc cat cca atc ctg tac ttc acc aat ggc cat 299  
 Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly His  
 70 75 80  
 ctg tat cca act ggt tct aag tca aag cgg gtc agc ctg ctt cag aac 347  
 30 Leu Tyr Pro Thr Gly Ser Lys Ser Lys Arg Val Ser Leu Leu Gln Asn  
 85 90 95  
 ccc ccc aca gtg ggg gtg gcc aca ctg aaa ctg act gac gtc cac ccc 395  
 Pro Pro Thr Val Gly Val Ala Thr Leu Lys Leu Thr Asp Val His Pro  
 100 105 110  
 35 tca gat act gga acc tac ctc tgc caa gtc aac aac cca cca gat ttc 443

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	Ser Asp Thr Gly Thr Tyr Leu Cys Gln Val Asn Asn Pro Pro Asp Phe	
	115 120 125	
	tac acc aat ggg ttg ggg cta atc aac ctt act gtg ctg gtt ccc ccc	491
	Tyr Thr Asn Gly Leu Gly Leu Ile Asn Leu Thr Val Leu Val Pro Pro	
5	130 135 140 145	
	agt aat ccc tta tgc agt cag agt gga caa acc tct gtg gga ggc tct	539
	Ser Asn Pro Leu Cys Ser Gln Ser Gly Gln Thr Ser Val Gly Gly Ser	
	150 155 160	
	act gca ctg aga tgc agc tct tcc gag ggg gct cct aag cca gtg tac	587
10	Thr Ala Leu Arg Cys Ser Ser Ser Glu Gly Ala Pro Lys Pro Val Tyr	
	165 170 175	
	aac tgg gtg cgt ctt gga act ttt cct aca cct tct cct ggc agc atg	635
	Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser Met	
	180 185 190	
15	gtt caa gat gag gtg tct ggc cag ctc att ctc acc aac ctc tcc ctg	683
	Val Gln Asp Glu Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser Leu	
	195 200 205	
	acc tcc tgg ggc acc tac cgc tgt gtg gcc acc aac cag atg ggc agt	731
	Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly Ser	
20	210 215 220 225	
	gca tcc tgt gag ctg acc ctc tct gtg acc gaa ccc tcc caa ggc cga	779
	Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly Arg	
	230 235 240	
	gtg gcc gga gct ctg att ggg gtg ctc ctg ggc gtg ctg ttg ctg tca	827
25	Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu Leu Ser	
	245 250 255	
	gtt gct ggc ttc tgc ctg gtc agg ttc cag aaa gag agg ggg aag aag	875
	Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Glu Arg Gly Lys Lys	
	260 265 270	
30	ccc aag gag aca tat ggg ggt agt gac ctt cgg gag gat gcc atc gct	923
	Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu Asp Ala Ile Ala	
	275 280 285	
	cct ggg atc tct gag cac act tgt atg agg gct gat tct agc aag ggg	971
	Pro Gly Ile Ser Glu His Thr Cys Met Arg Ala Asp Ser Ser Lys Gly	
35	290 295 300 305	

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ttc ctg gaa aga ccc tcg tot gcc agc acc gtg acg acc acc aag tcc 1019  
 Phe Leu Glu Arg Pro Ser Ser Ala Ser Thr Val Thr Thr Thr Lys Ser  
 310 315 320  
 aag etc cct atg gtc gtg tgactttctcc cgatccctga gggcggtgag ggg 1070  
 5 Lys Leu Pro Met Val Val  
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 gaatatcaat aattaaagtc tgtgggtacc 1100  
  
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 1 5 10 15  
 Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser  
 20 25 30  
 Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys  
 20 35 40 45  
 Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val  
 50 55 60  
 Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr  
 65 70 75 80  
 25 Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val  
 85 90 95  
 Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu  
 100 105 110  
 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala  
 30 115 120 125  
 Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala  
 130 135 140  
 Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His  
 145 150 155 160  
 35 Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu



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165 170 175  
 Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val  
 180 185 190  
 Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro  
 5 195 200 205  
 Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser  
 210 215 220  
 Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val  
 225 230 235 240  
 10 Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val  
 245 250 255  
 Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe  
 260 265 270  
 Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp  
 15 275 280 285  
 Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr  
 290 295 300  
 Glu Ala Ala Val Leu Leu Phe Tyr Arg  
 305 310  
 20  
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 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu  
 30 20 25 30  
 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe  
 35 40 45  
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val  
 50 55 60  
 35 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

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65                      70                      75                      80  
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr  
                                  85                      90                      95  
 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe  
 5                      100                      105                      110  
 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn  
                                  115                      120                      125  
 Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr  
                                  130                      135                      140  
 10 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile  
                                  145                      150                      155                      160  
 Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu  
                                  165                      170                      175  
 Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe  
 15                      180                      185                      190  
 Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val  
                                  195                      200                      205  
 Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys  
                                  210                      215                      220  
 20 Arg Lys Ser Arg Thr  
                                  225  
  
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 Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr  
                                  20                      25                      30  
 Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala  
                                  35                      40                      45  
 35 Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe

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	50	55	60
	Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys		
	65	70	75 80
5	Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro		
	85	90	95
	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe		
	100	105	110
	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr		
	115	120	125
10	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser		
	130	135	140
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp		
	145	150	155 160
	Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg		
15	165	170	175
	Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu		
	180	185	190
	Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys		
	195	200	205
20	Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val		
	210	215	220
	Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Ser		
	225	230	235 240
	Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr		
25	245	250	255
	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly		
	260	265	270
	Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro		
	275	280	285
30	His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr		
	290	295	300
	Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val		
	305	310	315 320
	Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Leu Met Asn		
35	325	330	335

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Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg  
 340 345 350  
 Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr  
 355 360 365  
 5 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val  
 370 375 380  
 Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu  
 385 390 395 400  
 Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile  
 10 405 410 415  
 Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn  
 420 425 430  
 Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu  
 435 440 445  
 15 Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr  
 450 455 460  
 Asn Val Ile  
 465  
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 25 <400> 34  
 Met Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser  
 1 5 10 15  
 Val Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu  
 20 25 30  
 30 Val Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro  
 35 40 45  
 Glu Thr Thr Thr Leu Thr Val Gly Gly Gly Val Phe Ala Leu Val Thr  
 50 55 60  
 Ala Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu  
 35 65 70 75 80

Phe Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Glu Lys Lys  
85 90 95  
Glu Val Leu

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5      <210> 35
      <211> 189
      <212> PRT
      <213> Homo sapiens

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      Leu Val Leu Ser Gly Ala Trp Gly Met Gln Met Trp Val Thr Phe Val
          20              25              30
15     Ser Gly Phe Leu Leu Phe Arg Ser Leu Pro Arg His Thr Phe Gly Leu
          35              40              45
      Val Gln Ser Lys Leu Phe Pro Phe Tyr Phe His Ile Ser Met Gly Cys
          50              55              60
      Ala Phe Ile Asn Leu Cys Ile Leu Ala Ser Gln His Ala Trp Ala Gln
20     65              70              75              80
      Leu Thr Phe Trp Glu Ala Ser Gln Leu Tyr Leu Leu Phe Leu Ser Leu
          85              90              95
      Thr Leu Ala Thr Val Asn Ala Arg Trp Leu Glu Pro Arg Thr Thr Ala
          100             105             110
25     Ala Met Trp Ala Leu Gln Thr Val Glu Lys Glu Arg Gly Leu Gly Gly
          115             120             125
      Glu Val Pro Gly Ser His Gln Gly Pro Asp Pro Tyr Arg Gln Leu Arg
          130             135             140
      Glu Lys Asp Pro Lys Tyr Ser Ala Leu Arg Gln Asn Phe Phe Arg Tyr
30     145             150             155             160
      His Gly Leu Ser Ser Leu Cys Asn Leu Gly Cys Val Leu Ser Asn Gly
          165             170             175
      Leu Cys Leu Ala Gly Leu Ala Leu Glu Ile Arg Ser Leu
          180             185
35

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<210> 36  
 <211> 363  
 <212> PRT  
 <213> Homo sapiens

5

&lt;400&gt; 36

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 Thr Phe Leu Arg Gly Ser Gln Thr Gln Ser His Pro Asp Leu Gly Thr  
 20 25 30  
 Glu Gly Cys Trp Asp Gln Leu Ser Ala Pro Arg Thr Phe Thr Leu Leu  
 35 40 45  
 Asp Pro Lys Ala Ser Leu Leu Thr Lys Ala Phe Leu Asn Gly Ala Leu  
 50 55 60  
 Asp Gly Val Ile Leu Gly Asp Tyr Leu Ser Arg Thr Pro Glu Pro Arg  
 65 70 75 80  
 Pro Ser Leu Ser His Leu Leu Ser Gln Tyr Tyr Gly Ala Gly Val Ala  
 85 90 95  
 Arg Asp Pro Gly Phe Arg Ser Asn Phe Arg Arg Gln Asn Gly Ala Ala  
 100 105 110  
 Leu Thr Ser Ala Ser Ile Leu Ala Gln Gln Val Trp Gly Thr Leu Val  
 115 120 125  
 Leu Leu Gln Arg Leu Glu Pro Val His Leu Gln Leu Gln Cys Met Ser  
 130 135 140  
 Gln Glu Gln Leu Ala Gln Val Ala Ala Asn Ala Thr Lys Glu Phe Thr  
 145 150 155 160  
 Glu Ala Phe Leu Gly Cys Pro Ala Ile His Pro Arg Cys Arg Trp Gly  
 165 170 175  
 Ala Ala Pro Tyr Arg Gly Arg Pro Lys Leu Leu Gln Leu Pro Leu Gly  
 180 185 190  
 Phe Leu Tyr Val His His Thr Tyr Val Pro Ala Pro Pro Cys Thr Asp  
 195 200 205  
 Phe Thr Arg Cys Ala Ala Asn Met Arg Ser Met Gln Arg Tyr His Gln  
 210 215 220  
 Asp Thr Gln Gly Trp Gly Asp Ile Gly Tyr Ser Phe Val Val Gly Ser

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225                      230                      235                      240  
 Asp Gly Tyr Val Tyr Glu Gly Arg Gly Trp His Trp Val Gly Ala His  
                          245                      250                      255  
 Thr Leu Gly His Asn Ser Arg Gly Phe Gly Val Ala Ile Val Gly Asn  
 5                      260                      265                      270  
 Tyr Thr Ala Ala Leu Pro Thr Glu Ala Ala Leu Arg Thr Val Arg Asp  
                          275                      280                      285  
 Thr Leu Pro Ser Cys Ala Val Arg Ala Gly Leu Leu Arg Pro Asp Tyr  
                          290                      295                      300  
 10    Ala Leu Leu Gly His Arg Gln Leu Val Arg Thr Asp Cys Pro Gly Asp  
                          305                      310                      315                      320  
 Ala Leu Phe Asp Leu Leu Arg Thr Trp Pro His Phe Thr Ala Thr Val  
                          325                      330                      335  
 Lys Pro Arg Pro Ala Arg Ser Val Ser Lys Arg Ser Arg Arg Glu Pro  
 15                      340                      345                      350  
 Pro Pro Arg Thr Leu Pro Ala Thr Asp Leu Gln  
                          355                      360  
  
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       <212> PRT  
       <213> Homo sapiens  
  
 <400> 37  
 25    Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala Gly Leu Leu Leu  
                          1                      5                      10                      15  
 Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr Arg Gly Arg Arg  
                          20                      25                      30  
 Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys Ser Ala Glu Asp  
 30                      35                      40                      45  
 Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala Glu Gln Leu Gln  
                          50                      55                      60  
 Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro Val Ile Ile Glu  
                          65                      70                      75                      80  
 35    Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe Ser Val Asn Gln

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	85	90	95
	Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val Ala Asn Lys Ile		
	100	105	110
	Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu Asn Ala Leu Asn		
5	115	120	125
	Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile Lys Val Gln Val		
	130	135	140
	Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala Met Thr Glu Gly		
	145	150	155
10	Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser Leu Tyr Asp Ser		
	165	170	175
	His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr Leu Phe Gln Asn		
	180	185	190
	Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala Val Gln Pro Thr		
15	195	200	205
	Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly Glu Glu Cys Ala		
	210	215	220
	Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala Glu Val Lys Glu		
	225	230	235
20	Lys Val Val Thr Ile Ile Pro Lys Ile		
	245		
	<210> 38		
	<211> 98		
25	<212> PRT		
	<213> Homo sapiens		
	<400> 38		
	Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile		
30	1	5	10
	Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe		
	20	25	30
	Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu		
	35	40	45
35	Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln		



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50                      55                      60  
 Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly  
 65                      70                      75                      80  
 Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met  
 5                      85                      90                      95  
 Val Arg  
  
 <210> 39  
 <211> 172  
 10 <212> PRT  
 <213> Homo sapiens  
  
 <400> 39  
 Met Val Gly Pro Ala Pro Arg Arg Arg Leu Arg Pro Leu Ala Ala Leu  
 15     1                      5                      10                      15  
 Ala Leu Val Leu Ala Leu Ala Pro Gly Leu Pro Thr Ala Arg Ala Gly  
 20                      20                      25                      30  
 Gln Thr Pro Arg Pro Ala Glu Arg Gly Pro Pro Val Arg Leu Phe Thr  
 35                      40                      45  
 20 Glu Glu Glu Leu Ala Arg Tyr Gly Gly Glu Glu Glu Asp Gln Pro Ile  
 50                      55                      60  
 Tyr Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu  
 65                      70                      75                      80  
 Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser  
 25                      85                      90                      95  
 Thr Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His  
 100                      105                      110  
 Asp Thr Thr Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Glu Val  
 115                      120                      125  
 30 Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala  
 130                      135                      140  
 Arg Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro  
 145                      150                      155                      160  
 Glu Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe  
 35                      165                      170

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<210> 40  
 <211> 120  
 <212> PRT  
 5 <213> Homo sapiens  
  
 <400> 40  
 Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser Ser Lys  
 1 5 10 15  
 10 Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile Asp Leu  
 20 25 30  
 Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile Ala Leu  
 35 40 45  
 Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile Gly Ser  
 15 50 55 60  
 Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg Ala Val  
 65 70 75 80  
 Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe Tyr His  
 85 90 95  
 20 Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr Ser Tyr  
 100 105 110  
 Asp Asp Ile Pro Asp Phe Asp Asp  
 115 120  
  
 25 <210> 41  
 <211> 939  
 <212> DNA  
 <213> Homo sapiens  
  
 30 <400> 41  
 atgaaccaac tcagcttccg gctgtttctc atagcgacca ccagaggatg gactacagat 60  
 gagggctaata cttacttcaa ggaatggacc tgtttctctg ctccatctct gccagaagc 120  
 tgcaaggaaa tcaagacga atgtcctagt gcatttgatg gcctgtatct tctccgact 180  
 gagaatggtg ttatctacca gaccttctgt gacatgacct ctgggggtgg cggtggacc 240  
 35 ctggtggcca gcgtgcata gaatgacatg cgtgggaagt gcacgggtgg cgatcgtgg 300

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tccagtcagc agggcagcaa agcagactac ccagaggggg acggcaactg ggccaactac 360  
 aacacctttg gatctgcaga ggcggccacg agcgtatgact acaagaaccc tggtactac 420  
 gacatccagg ccaaggacct gggcatctgg cacgtgccca ataagteccc catgcagcac 480  
 tggagaaaca gctccctgct gaggtaccgc acggacactg gcttcctcca gacactggga 540  
 5 cataatctgt ttggcatcta ccagaaatat ccagtgaat atggagaagg aaagtgttg 600  
 actgacaaag gcccggtgat cctgtggtc tatgattttg gcgacgcca gaaaaagca 660  
 tcttattact caccctatgg ccagcgggaa ttcactcggg gatttgttca gttcagggt 720  
 tttataaacg agagagcagc caacgccttg tgtgtggaa tgagggtcac cggatgtaac 780  
 actgagcacc actgcattgg tggaggagga tactttccag aggcagtc ccagcagtg 840  
 10 ggagattttt ctggtttga ttggagtggg tatggaactc atgttggtta cagcagcagc 900  
 cgtgagataa ctgaggcagc tgtgttcta ttctatcgt 939

&lt;210&gt; 42

&lt;211&gt; 687

15 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 42

atgggcgaca agatctggct gcccttccc gtgtctcttc tggcgcctct gcctccggtg 60  
 20 ctgtgcctg gggcgccggg ctccacacct tccctcgata ggcacttcac ctttaacctt 120  
 cccgcgggco agaaggagtg cttctaccag cccatgccc tgaaggctc gctggagatc 180  
 gagtaccaag ttttagatgg agcaggatta gatattgatt tccatcttgc ctctccagaa 240  
 ggcaaaacct tagttttga acaagaaaa tcagatggag ttcactctgt agagactgaa 300  
 gttggtgatt acatgttctg ctttgacaat acattcagca ccatttctga gaaggtgatt 360  
 25 ttctttgaat taactctgga taatatggga gaacaggcac aagaacaaga agattggaag 420  
 aaatatatta ctggcacaga tatattgat atgaaactgg aagacatcct ggaatccatc 480  
 aacagcaca agtcagact aagcaaaagt gggcacatac aaattctgct tagagcattt 540  
 gaagctcgtg atcgaaacat acaagaaagc aactttgata gagtcaattt ctggtctatg 600  
 gtttaatttag tggtcattgt ggtggtgtca gccattcaag tttatatgct gaagagtctg 660  
 30 tttgaagata agaggaaaag tagaact 687

&lt;210&gt; 43

&lt;211&gt; 1401

&lt;212&gt; DNA

35 &lt;213&gt; Homo sapiens

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<400> 43  
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 ctgccgcgcg cgccgtgccc tgcccacagc gccacgcgct tcgaccccac ctgggagctc 120  
 5 ctggacgccc gccagctgcc cgcgtgggtt gaccaggcca agttcggcat ctccatccac 180  
 tggggagtgt tttccgtgcc cagcttcggt agcagtggtt tctggtggta ttggcaaaag 240  
 gaaaagatac cgaagtatgt ggaatttatg aaagataatt acctcctag tttcaaatat 300  
 gaagattttg gaccactatt tacagcaaaa ttttttaatg ccaaccagtg ggcagatatt 360  
 tttcaggcct ctggtgccaa atacattgtc ttaacttcca aacatcatga aggcctttacc 420  
 10 ttgtgggggt cagaatatto gtggaactgg aatgccatag atgagggggc caagagggac 480  
 attgtcaagg aacttgaggt agccattagg aacagaactg acctgcgttt tggactgtac 540  
 tattcccttt ttgaatgggt tcatccgctc ttccttgagg atgaatccag ttcattccat 600  
 aagcggcaat ttccagtctc taagacattg ccagagctct atgagttagt gaacaactat 660  
 cagcctgagg ttctgtggtc ggatggtgac ggaggagcac cggatcaata ctggaaacagc 720  
 15 acaggcttct tggcctggtt atataatgaa agcccagttc ggggcacagt agtcccaat 780  
 gatcgttggg gagctggtag catctgtaag catggtggct tctataacctg cagtgatect 840  
 tataaccacg gacatctttt gccacataaa tgggaaaact gcatgacaat agacaactg 900  
 tcttggggct ataggaggga agctggaatc tctgactatc ttacaattga agaattgggtg 960  
 aagcaacttg tagagacagt ttcattgtga ggaatctttt tgatgaatat tggggccaca 1020  
 20 ctatagtgga ccatttctgt agtttttgag gagcgactga ggcaaatggg gtccctggta 1080  
 aaagtcaatg gagaagctat ttatgaaacc catacctggc gatcccagaa tgacactgtc 1140  
 accccagatg tgtggtacac atccaagcct aaagaaaaat tagtctatgc cttttttctt 1200  
 aaatggccca catcaggaca gctgttcctt ggccatccca aagctattct gggggcaaca 1260  
 gaggtgaac tactgggaca tggaoagoca cttaactgga tttctttgga gcaaatggc 1320  
 25 attatggtag aactgccaca gctaaccatt catcagatgc cgtgtaaatg gggctgggct 1380  
 ctagccctga ctaatgtgat c 1401

<210> 44  
 <211> 297  
 30 <212> DNA  
 <213> Homo sapiens

<400> 44  
 atggataacg tgcagccgaa aataaaacat cgcctcttct gcttcagtgt gaaaggccac 60  
 35 gtgaagatgc tgcggtgga tattatcaac tcaactggta caacagtatt catgctcacc 120

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	gtatctgtgt tggcactgat accagaaacc acaacattga cagttggtgg aggggtgttt	180
	gcacttgtga cagcagtatg ctgtcttgcc gacggggccc ttatttaccg gaagcttctg	240
	ttcaatccca gcggtcctta ccagcaaaag cctgtgcatg aaaaaaaga agttttg	297
5	<210> 45	
	<211> 567	
	<212> DNA	
	<213> Homo sapiens	
10	<400> 45	
	atggaggaag gcgggaacct aggaggcctg attaagatgg tccatctact ggtcttgtca	60
	ggtgcctggg gcctgcaaat gtyggtgacc ttcgtctcag gcttcctgot ttccggaagc	120
	cttccccgac ataccttcgg actagtgcag agcaaaactct tcccttcta ctccacatc	180
	tccatgggct gtgccttcat caacctctgc atcttggctt caccagatgc ttgggctcag	240
15	ctcacattct gggaggccag ccagctttac ctgctgttcc tgagccttac gctggcact	300
	gtcaacgccc gctggctgga accccgcacc acagctgcca tgtgggccct gcaaacctg	360
	gagaaggagc gaggcctggg tggggaggta ccaggcagcc accagggctc cgatccctac	420
	cgccagctgc gagagaagga ccccaagtac agtgcctccc gccagaattt ctcccgctac	480
	catgggctgt cctctctttg caatctgggc tgcgtcctga gcaatgggct ctgtctcgt	540
20	ggccttgcgc tggaaataag gacccctc	567
	<210> 46	
	<211> 1089	
	<212> DNA	
25	<213> Homo sapiens	
	<400> 46	
	atgggtggaca gctcctggc agtcacctg gctggaaacc tgggcctgac cttectccga	60
	ggttcccaga ccagagcca tccagaactg ggaactgagg gctgctggga ccagctctct	120
30	gcccctcgga cctttacgt tttggaccc aaggcatctc tgttaaccac ggccttctc	180
	aatggcgccc tggatggggt catccttggg gactacctga gccggactcc tgagccccgg	240
	ccatccctca gccacttct gaggcagta tatggggctg ggggtggccag agaccaggg	300
	ttccgcagca acttccgacg gcagaacggt gctgctctga ctccagctcc catcctggcc	360
	cagcaggtgt ggggaacct tgtccttcta cagaggtgg agccagtaca cctccagctt	420
35	cagtgcctga gccaaagaca gctggcccag gtggctgcca atgctaccaa ggaattcact	480

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gaggccttcc tgggatgcc ggccatccac ccccgctgcc gctggggagc ggcgccttat 540  
 cggggccgcc cgaagctgct gcagctgccg ctgggattct tgtacgtgca tcacacctac 600  
 gtgctctgac caccctgac ggacttcacg cgtgctgag ccaacatgcy ctccatgcag 660  
 cgtaccacac aggcacgcga aggctgggga gacatcggct acagtctcgt ggtgggctcg 720  
 5 gacggctacg tgtacgaggg acgcggctgg cactgggtgg ggcgccacac gctgggcac 780  
 aaactccggg gcttcggcgt ggccatagtg ggcaactaca ccgcggcgct gccaccgcag 840  
 gccgctctgc gcacggctgc cgacacgctc ccgagttgtg cggtycgcygc cggcctctcg 900  
 cggccagact acgcgctgct ggccaccgc cagctggtgc gcaccgactg ccccggcgac 960  
 gcgctcttcg acctgctgcg cactggcgc cacttcaccg cgactgttaa gccaaacct 1020  
 10 gccaggagtg tctctaagag atccaggagg gagccacccc caaggacct gccagccaca 1080  
 gacctccaa 1089

&lt;210&gt; 47

&lt;211&gt; 747

15 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

atgggtggcc cccggggcgc gggtgggtg gggcgggccc tctgtctcgg cgcggggcgc 60  
 20 tgcactgca ttacaggct gacccgggt cggcgggcgg gcgaccgcga gctcgggata 120  
 cgtctctcga agtcgcaga agacttaact gatggttcat atgatgatgt tctaatgct 180  
 gaacaacttc aqaactcct ttacctgctg gagtcaacgg aggatcctgt aattattgaa 240  
 agagctttga ttactttggg taacaatgca gccttttcag ttaaccaagc tattattcgt 300  
 gaattgggtg gtattccaat tgttgcaaac aaaatcaacc attccaacca gagtattaaa 360  
 25 gagaagctt taaatgcact aaataacctg agtgtgaatg ttgaaatca aatcaagata 420  
 aagggtgcaag ttttgaact gcttttgaat ttgtctgaaa atccagccat gacagaagga 480  
 cttctccgtg cccaagtga ttcatcattc ctttcccttt atgacagcca cgtagcaaaag 540  
 gagattcttc ttgcagtact tacgtatatt cagaatataa agaactgcct caaatagaa 600  
 ggccatttag ctgtgcagcc tactttcact gaaggttcat tgttttccct gttacatgga 660  
 30 gaagaatgtg cccagaaaat aagagcttta gttgatcacc atgatgcaga ggtgaaggaa 720  
 aagggtgtaa caataatacc caaantc 747

&lt;210&gt; 48

&lt;211&gt; 294

35 &lt;212&gt; DNA

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&lt;213&gt; Homo sapiens

&lt;400&gt; 48

5 atggcgtegc tcctgtgctg tgggcogaag ctggcgcct gcggcatcgt cctcagcgcc 60  
 tggggagtga tcattgtgat aatgetcgga atatttttca atgtccattc cgtgtgttg 120  
 attgaggacg ttcccttcac ggagaaagat ttgagaatg gccccagaa catatacaac 180  
 ctttacgagc aagtcagcta caactgttcc atcgtgcag gcctttacct cctcctcgga 240  
 ggcttctctt tctgccaagt tgggtccaat aagcgcaagg aatacatggt gcgc 294

10 &lt;210&gt; 49

&lt;211&gt; 516

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

15 &lt;400&gt; 49

atggcgggccc cgcgcgcgcg gcggcggctg cggccgctgy cagcgtggc cctggctctg 60  
 gcgcrggccc cggggctgcc cacagcccgg gccgggcaga caccgcgcgc tgcgagcgg 120  
 gggccccag tgcggctttt cacagaggag gagctggccc gctatggcgg ggaggaggaa 180  
 gatcagccca tctacttggc agtgaaggga gtggtgttg atgtaccctc cggaaaggag 240  
 20 ttttatggac gaggagcccc ctacaatgcc ttgacgggga aggaactccac tagaggggta 300  
 gccaaagatgt ccttggatcc tgcagacctc acccatgaca ctacgggtct caccggccag 360  
 gaactggagg ccctggatga ggtcttcacc aaagtgtaca aagccaaata ccccatcgtc 420  
 ggctacactg cccggagaat tctcaatgag gatggcagcc ctaacctgga cttcaagcct 480  
 gaagaccagc cccattttga catcaaggat gagttc 516

25

&lt;210&gt; 50

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

30

&lt;400&gt; 50

atgatgccgt cccgtaccaa cctggctact ggaatcccca gtagtaaggt gaaatattca 60  
 aggetctcca gcacagacga tggtacatt gacctcagt ttaagaaaac cctcctaag 120  
 atcccttata aggcctcgc acttgccact gtgctgtttt tgattggcgc ctttctcatt 180  
 35 attatacgct cctcctgct gtcaggctac atcagcaag ggggggcaga ccgggcctg 240

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ccagtgtga tcattggcat tctggtgttc ctaccggat ttaccacct gcgcacgct 300  
tactatgcat ccaaaggcta ccgtggttac tctatgatg acattccaga ctttgatgac 360

<210> 51  
5 <211> 1065  
<212> DNA  
<213> Homo sapiens  
<220>  
<221> CDS  
10 <222> (2)...(943)

<400> 51  
a atg aac caa ctc agc ttc ctg ctg ttt ctc ata gcg acc acc aga gga 49  
Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg Gly  
15 1 5 10 15  
tgg agt aca gat gag gct aat act tac ttc aag gaa tgg acc tgt tct 97  
Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser  
20 20 25 30  
tcg tct cca tct ctg ccc aga agc tgc aag gaa atc aaa gac gaa tgt 145  
Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys  
25 35 40 45  
cct agt gca ttt gat ggc ctg tat ttt ctc cgc act gag aat ggt gtt 193  
Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val  
50 55 60  
atc tac cag acc ttc tgt gac atg acc tct ggg ggt ggc ggc tgg acc 241  
Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr  
65 70 75 80  
ctg gtg gcc agc gtg cat gag aat gac atg cgt ggg aag tgc acg gtg 289  
Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val  
30 85 90 95  
ggc gat cgc tgg tcc agt cag cag ggc agc aaa gca gac tac cca gag 337  
Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu  
100 105 110  
ggg gac ggc aac tgg gcc aac tac aac acc ttt gga tct gca gag gcg 385  
35 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala



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	115	120	125	
	gcc acg agc gat gac tac aag aac cct gcc tac tac gac atc cag gcc	433		
	Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala			
	130	135	140	
5	aag gac ctg gcc atc tgg cac gtg ccc aat aag tcc ccc atg cag cac	481		
	Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His			
	145	150	155	160
	tgg aga aac agc tcc ctg ctg agg tac cgc acg gac act gcc ttc ctc	529		
	Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu			
10	165	170	175	
	cag aca ctg gga cat aat ctg ttt gcc atc tac cag aaa tat cca gtg	577		
	Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val			
	180	185	190	
	aaa tat gga gaa gga aag tgt tgg act gac aac gcc ccg gtg atc cct	625		
15	Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro			
	195	200	205	
	gtg gtc tat gat ttt gcc gac gcc cag aaa aca gca tct tat tac tca	673		
	Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser			
	210	215	220	
20	ccc tat gcc cag cgg gaa ttc act gcg gga ttt gtt cag ttc agg gta	721		
	Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val			
	225	230	235	240
	ttt aat aac gag aga gca gcc aac gcc ttg tgt gct gga atg agg gtc	769		
	Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val			
25	245	250	255	
	acc gga tgt aac act gag cac cac tgc att ggt gga gga tac ttt	817		
	Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe			
	260	265	270	
	cca gag gcc agt ccc cag cag tgt gga gat ttt tct ggt ttt gat tgg	865		
30	Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp			
	275	280	285	
	agt gga tat gga act cat gtt ggt tac agc agc agc cgt gag ata act	913		
	Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr			
	290	295	300	
35	gag gca gct gtg ctt cta ttc tat cgt tgagagtttt gtgggagggg	960		

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Glu Ala Ala Val Leu Leu Phe Tyr Arg  
 305 310  
 acccagacct ctctctccaa ccatgagatc ccaaggatgg agaacaactt acccagtagc 1020  
 tagaatgtta atggcagaag agaaaacaat aaatcatatt gactc 1065

5  
 <210> 52  
 <211> 937  
 <212> DNA  
 <213> Homo sapiens

10  
 <220>  
 <221> CDS  
 <222> (177)...(866)

<400> 52

15 cttttggaga actgcgttc tcttggag ggagtgttcg ccgcgcgcgc gccgcgcacc 60  
 tggagtttct teagactcca gattccctg tcaaccacga ggagtccaga gaggaacgc 120  
 ggagcggaga caacagtacc tgacgctct ttcagcccg gatgcacca gcaggg 176  
 atg ggc gac aag atc tgg ctg ccc ttc ccc gtg ctc ctt ctg gcc gct 224  
 Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala

20 1 5 10 15  
 ctg cct ccg gtg ctg ctg cct ggg gcg gcc gcc ttc aca cct tcc ctc 272  
 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu

25 20 25 30  
 gat agc gac ttc acc ttt acc ctt ccc gcc gcc cag aag gag tgc ttc 320  
 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe

35 40 45  
 tac cag ccc atg ccc ctg aag gcc tcg ctg gag atc gag tac caa gtt 368  
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val

50 55 60  
 tta gat gga gca gga tta gat att gat ttc cat ctt gcc tct cca gaa 416  
 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

65 70 75 80  
 ggc aaa acc tta gtt ttt gaa caa aga aaa tca gat gga gtt cac act 464  
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr

35 85 90 95

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	gta gag act gaa gtt ggc gat tac atg ttc tgc ttt gac aat aca ttc	512
	Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe	
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	agc acc att tct gag aag gtg att ttc ttt gaa tta atc ctg gat aat	560
5	Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn	
	115 120 125	
	atg gga gaa cag gca caa gaa caa gaa gat tgg aag aaa tat att act	608
	Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr	
	130 135 140	
10	ggc aca gat ata ttg gat atg aaa ctg gaa gac atc ctg gaa tcc atc	656
	Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile	
	145 150 155 160	
	aac agc atc aag tcc aga cta agc aaa agt ggg cac ata caa att ctg	704
	Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu	
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	ctt aga gca ttt gaa gct cgt gat cga aac ata caa gaa agc aac ttt	752
	Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe	
	180 185 190	
	gat aga gtc aat ttc tgg tct atg gtt aat tta gtg gto atg gtg gtg	800
20	Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val	
	195 200 205	
	gtg tca gcc att caa gtt tat atg ctg aag agt ctg ttt gaa gat aag	848
	Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys	
	210 215 220	
25	agg aaa agt aga act taaaactcca aactagagta cgtaacattg aaaaatg	900
	Arg Lys Ser Arg Thr	
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	aggcataaaa atgcaataaa ctgttacagt caagacc	937
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	Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu	
	1 5 10 15	
	ctg ttg ctg ctg ctg ccg ccg ccg ccg tgc cct gcc cac agc gcc acg	151
	Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr	
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	cgc ttc gac ccc acc tgg gag tcc ctg gac gcc cgc cag ctg ccc gcg	199
	Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala	
	35 40 45	
	tgg ttt gac cag gcc aag ttc ggc atc ttc atc cac tgg gga gtg ttt	247
15	Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe	
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	tcc gtg ccc agc ttc ggt agc gag tgg ttc tgg tgg tat tgg caa aag	295
	Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys	
	65 70 75 80	
20	gaa aag ata ccg aag tat gtg gaa ttt atg aaa gat aat tac cct cct	343
	Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro	
	85 90 95	
	agt ttc aaa tat gaa gat ttt gga cca cta ttt aca gca aaa ttt ttt	391
	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe	
25	100 105 110	
	aat gcc aac cag tgg gca gat att ttt cag gcc tct ggt gcc aaa tac	439
	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	
	115 120 125	
	att gtc tta act tcc aaa cat cat gaa ggc ttt acc ttg tgg ggg tca	487
30	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser	
	130 135 140	
	gaa tat tgg tgg aac tgg aat gcc ata gat gag ggg ccc aag agg gac	535
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp	
	145 150 155 160	
35	att gtc aag gaa ctt gag gta gcc att agg aac aga act gac ctg cgt	583

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	ttt gga ctg tac tat tcc ctt ttt gaa tgg ttt cat ccg ctc ttc ctt	631
	Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu	
5	180 185 190	
	gag gat gaa tcc agt tca ttc cat aag cgg caa ttt cca gtt tct aag	679
	Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys	
	195 200 205	
	aca ttg cca gag ctc tat gag tta gtg aac aac tat cag cct gag gtt	727
10	Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val	
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	ctg tgg tcc gat ggt gac gga gga gca ccg gat caa tac tgg aac agc	775
	Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Ser	
	225 230 235 240	
15	aca ggc ttc ttg gcc tgg tta tat aat gaa agc cca gtt cgg ggc aca	823
	Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr	
	245 250 255	
	gta gtc acc aat gat cgt tgg gga gct ggt agc atc tgt aag cat ggt	871
	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly	
20	260 265 270	
	ggc ttc tat acc tgc agt gat cgt tat aac cca gga cat ctt ttg cca	919
	Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro	
	275 280 285	
	cat aaa tgg gaa aac tgc atg aca ata gac aaa ctg tcc tgg ggc tat	967
25	His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr	
	290 295 300	
	agg agg gaa gct gga atc tct gac tat ctt aca att gaa gaa ttg gtg	1015
	Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val	
	305 310 315 320	
30	aag caa ctt gta gag aca gtt tca tgt gga gga aat ctt ttg atg aat	1063
	Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Leu Met Asn	
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	att ggg ccc aca cta gat ggc acc att tct gta gtt ttt gag gag cga	1111
	Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg	
35	340 345 350	

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Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr
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gaa acc cat acc tgg cga tcc cag aat gac act gtc acc cca gat gtg      1207
5  Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val
      370              375              380
tgg tac aca tcc aag cct aaa gaa aaa tta gtc tat gcc att ttt ctt      1255
Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu
      385              390              395              400
10  aaa tgg ccc aca tca gga cag ctg ttc ctt ggc cat ccc aaa gct att      1303
Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile
      405              410              415
ctg ggg gca aca gag gtg aaa cta ctg ggc cat gga cag cca ctt aac      1351
Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn
15      420              425              430
tgg att tot ttg gag caa aat ggc att atg gta gaa ctg cca cag cta      1399
Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu
      435              440              445
acc att cat cag atg ccg tgt aaa tgg ggc tgg gct cta gcc ctg act      1447
20  Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr
      450              455              460
aat gtg atc taaagtgcag cagagtggct gatgctgcaa gttatgteta aggc      1500
Asn Val Ile
465
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agaaaattat tttggcagtt cagcccttcc cctttttccc actaaatttt ttcttaaatt      1620
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5                                     Met
                                     1
gat aac gtg cag ccg aaa ata aaa cat cgc ccc ttc tgc ttc agt gtg      164
Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val
                                     5          10          15
10 aaa ggc cac gtg aag atg ctg cgg ctg gat att atc aac tca ctg gta      212
Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu Val
                                     20          25          30
aca aca gta ttc atg ctc atc gta tct gtg ttg gca ctg ata cca gaa      260
Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Glu
15          35          40          45
acc aca aca ttg aca gtt ggt gga ggg gtg ttt gca ctt gtg aca gca      308
Thr Thr Thr Leu Thr Val Gly Gly Gly Val Phe Ala Leu Val Thr Ala
          50          55          60          65
20 gta tgc tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc      356
Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe
          70          75          80
aat ccc agc ggt cct tac cag caa aag cct gtg cat gaa aaa aaa gaa      404
Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Glu Lys Lys Glu
          85          90          95
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Val Leu

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	gggtgctgcg gattgaggtc ccggttcta acgaatctct gctggatttg ccgtaacct	180
	gtcccgagc gggctcacag ggtctgaagg ccacgatga ggcaaggta aagttctgag	240
	ccaccgggtg cctccttccc aggaactgcaa g atg gag gaa ggc ggg aac cta	292
	Met Glu Glu Gly Gly Asn Leu	
10	1 5	
	gga ggc ctg att aag atg gtc cat cta ctg gtc ttg tca ggt gcc tgg	340
	Gly Gly Leu Ile Lys Met Val His Leu Leu Val Leu Ser Gly Ala Trp	
	10 15 20	
	ggc atg caa atg tgg gtg acc ttc gtc tca ggc ttc ctg ctt ttc cga	388
15	Gly Met Gln Met Trp Val Thr Phe Val Ser Gly Phe Leu Leu Phe Arg	
	25 30 35	
	agc ctt ccc cga cat acc ttc gga cta gtg cag agc aaa ctc ttc ccc	436
	Ser Leu Pro Arg His Thr Phe Gly Leu Val Gln Ser Lys Leu Phe Pro	
	40 45 50 55	
20	ttc tac ttc cac atc tcc atg ggc tgt gcc ttc atc aac ctc tgc atc	484
	Phe Tyr Phe His Ile Ser Met Gly Cys Ala Phe Ile Asn Leu Cys Ile	
	60 65 70	
	ttg gct tca cag cat gct tgg gct cag ctc aca ttc tgg gag gcc agc	532
	Leu Ala Ser Gln His Ala Trp Ala Gln Leu Thr Phe Trp Glu Ala Ser	
25	75 80 85	
	cag ctt tac ctg ctg ttc ctg agc ctt acg ctg gcc act gtc aac gcc	580
	Gln Leu Tyr Leu Leu Phe Leu Ser Leu Thr Leu Ala Thr Val Asn Ala	
	90 95 100	
	cgc tgg ctg gaa ccc cgc acc aca gct gcc atg tgg gcc ctg caa acc	628
30	Arg Trp Leu Glu Pro Arg Thr Thr Ala Ala Met Trp Ala Leu Gln Thr	
	105 110 115	
	gtg gag aag gag cga ggc ctg ggt ggg gag gta cca ggc agc cac cag	676
	Val Glu Lys Glu Arg Gly Leu Gly Gly Glu Val Pro Gly Ser His Gln	
	120 125 130 135	
35	ggg ccc gat ccc tac cgc cag ctg cga gag aag gac ccc aag tac agt	724



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	aag gcc ttc ctc aat ggc gcc ctg gat ggg gtc atc ctt gga gac tac	365
	Lys Ala Phe Leu Asn Gly Ala Leu Asp Gly Val Ile Leu Gly Asp Tyr	
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	ctg agc cgg act cct gag ccc cgg cca tcc ctc agc cac ttg ctg agc	413
5	Leu Ser Arg Thr Pro Glu Pro Arg Pro Ser Leu Ser His Leu Leu Ser	
	75 80 85	
	cag tac tat ggg gct ggg gtg gcc aga gac cca ggg ttc cgc ago aac	461
	Gln Tyr Tyr Gly Ala Gly Val Ala Arg Asp Pro Gly Phe Arg Ser Asn	
	90 95 100	
10	ttc cga cgg cag aac ggt gct gct ctg act tca gcc tcc atc ctg gcc	509
	Phe Arg Arg Gln Asn Gly Ala Ala Leu Thr Ser Ala Ser Ile Leu Ala	
	105 110 115 120	
	cag cag gtg tgg gga acc ctt gtc ctt cta cag agg ctg gag cca gta	557
	Gln Gln Val Trp Gly Thr Leu Val Leu Leu Gln Arg Leu Glu Pro Val	
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	His Leu Gln Leu Gln Cys Met Ser Gln Glu Gln Leu Ala Gln Val Ala	
	140 145 150	
	gcc aat gct acc aag gaa ttc act gag gcc ttc ctg gga tgc cgc gcc	653
20	Ala Asn Ala Thr Lys Glu Phe Thr Glu Ala Phe Leu Gly Cys Pro Ala	
	155 160 165	
	atc cac ccc cgc tgc cgc tgg gga gcg gcg cct tat cgg ggc cgc ccg	701
	Ile His Pro Arg Cys Arg Trp Gly Ala Ala Pro Tyr Arg Gly Arg Pro	
	170 175 180	
25	aag ctg ctg cag ctg cgc ctg gga ttc ttg tac gtg cat cac acc tac	749
	Lys Leu Leu Gln Leu Pro Leu Gly Phe Leu Tyr Val His His Thr Tyr	
	185 190 195 200	
	gtg cct gca cca ccc tgc acg gac ttc acg cgc tgc gca gcc aac atg	797
	Val Pro Ala Pro Pro Cys Thr Asp Phe Thr Arg Cys Ala Ala Asn Met	
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	cgc tcc atg cag cgc tac cac cag gac acg caa ggc tgg gga gac atc	845
	Arg Ser Met Gln Arg Tyr His Gln Asp Thr Gln Gly Trp Gly Asp Ile	
	220 225 230	
	ggc tac agt ttc gtg gtg ggc tgc gac ggc tac gtg tac gag gga cgc	893
35	Gly Tyr Ser Phe Val Val Gly Ser Asp Gly Tyr Val Tyr Glu Gly Arg	

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	235	240	245	
	ggc tgg cac tgg gtg ggc gcc cac acg ctc ggc cac aac tcc cgg ggc			941
	Gly Trp His Trp Val Gly Ala His Thr Leu Gly His Asn Ser Arg Gly			
	250	255	260	
5	ttc ggc gtg gcc ata gtg ggc aac tac acc gcg gcg ctg ccc acc gag			989
	Phe Gly Val Ala Ile Val Gly Asn Tyr Thr Ala Ala Leu Pro Thr Glu			
	265	270	275	280
	gcc gct ctg cgc acg gtg cgc gac acg ctc ccg agt tgt gcg gtg cgc			1037
	Ala Ala Leu Arg Thr Val Arg Asp Thr Leu Pro Ser Cys Ala Val Arg			
10		285	290	295
	gcc ggc ctc ctg cgg cca gac tac gcg ctg ctg ggc cac cgc cag ctg			1085
	Ala Gly Leu Leu Arg Pro Asp Tyr Ala Leu Leu Gly His Arg Gln Leu			
	300	305	310	
	gtg cgc acc gac tgc ccc ggc gac gcg ctc ttc gac ctg ctg cgc acc			1133
15	Val Arg Thr Asp Cys Pro Gly Asp Ala Leu Phe Asp Leu Leu Arg Thr			
	315	320	325	
	tgg ccg cac ttc acc gcg act gtt aag cca aga cct gcc agg agt gtc			1181
	Trp Pro His Phe Thr Ala Thr Val Lys Pro Arg Pro Ala Arg Ser Val			
	330	335	340	
20	tct aag aga tcc agg agg gag cca ccc cca agg acc ctg cca gcc aca			1229
	Ser Lys Arg Ser Arg Arg Glu Pro Pro Pro Arg Thr Leu Pro Ala Thr			
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	gccgcggcgg cagc atg ggt ggc ccc cgg ggc gcg ggc tgg gtg gcg gcg	170
	Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala	
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5	ggc ctg ctg ctc ggc gcg ggc gcc tgc tac tgc att tac agg ctg acc	218
	Gly Leu Leu Leu Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr	
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	cgg ggt cgg cgg cgg ggc gac cgc gag ctc ggg ata cgc tct teg aag	266
	Arg Gly Arg Arg Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys	
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	tcc gca gaa gac tta act gat ggt tca tat gat gat gtt cta aat gct	314
	Ser Ala Glu Asp Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala	
	45 50 55 60	
	gaa caa ctt cag aaa ctc ctt tac ctg ctg gag tca acg gag gat cct	362
15	Glu Gln Leu Gln Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro	
	65 70 75	
	gta att att gaa aga gct ttg att act ttg ggt aac aat gca gcc ttt	410
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20	tca gtt aac caa gct att att cgt gaa ttg ggt ggt att cca att gtt	458
	Ser Val Asn Gln Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val	
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	gca aac aaa etc aac cat tcc aac cag agt att aaa gag aaa gct tta	506
	Ala Asn Lys Ile Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu	
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	aat gca cta aat aac ctg agt gtg aat gtt gaa aat caa atc aag ata	554
	Asn Ala Leu Asn Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile	
	125 130 135 140	
	aag gtg caa gtt ttg aaa ctg ctt ttg aat ttg tct gaa aat cca gcc	602
30	Lys Val Gln Val Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala	
	145 150 155	
	atg aca gaa gga ctt ctc cgt gcc caa gtg gat tca tca ttc ctt tcc	650
	Met Thr Glu Gly Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser	
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35	ctt tat gac agc cac gta gca aag gag att ctt ctt cga gta ctt acg	698

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 Leu Phe Gln Asn Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala  
 5 190 195 200  
 gtg cag cct act ttc act gaa ggt tca ttg ttt ttc ctg tta cat gga 794  
 Val Gln Pro Thr Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly  
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 gaa gaa tgt gcc cag aaa ata aga gct tta gtt gat cac cat gat gca 842  
 10 Glu Glu Cys Ala Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala  
 225 230 235  
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 Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile Val Leu Ser  
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 gcc tgg gga gtg atc atg ttg ata atg ctc gga ata ttt ttc aat gtc 152  
 Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe Phe Asn Val  
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	gag aat ggc ccc cag aac ata tac aac ctt tac gag caa gtc agc tac			248
	Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln Val Ser Tyr			
	55	60	65	
5	aac tgt ttc atc gct gca ggc ctt tac ctc ctc ctc gga ggc ttc tct			296
	Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly Gly Phe Ser			
	70	75	80	
	ttc tgc caa gtt cgg ctc aat aag cgc aag gaa tac atg gtg cgc			341
	Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met Val Arg			
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	gtgtcaccca ggtagcgtcc cacccttgcc ggagcctct gtgggactgg gtttccggg			460
	cgagagactg aatcccttct cccatctctg gcatecggcc cccgtggaga gggetgagge			520
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	10	15	20	25
	ctg ccc aca gcc cgg gcc ggg cag aca ccg cgc cct gcc gag cgg ggg			147
	Leu Pro Thr Ala Arg Ala Gly Gln Thr Pro Arg Pro Ala Glu Arg Gly			
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5	gccaaaccgtg ggcgagctct ggggtgtgcgg gcggcctggc gcggcgtcc gctgtgtcag	120
	cgtgtt atg atg ccg tcc cgt acc aac ctg gct act gga atc ccc agt	168
	Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser	
	1 5 10	
	agt aaa gtg aaa tat tca agg ctc tcc agc aca gac gat ggc tac att	216
10	Ser Lys Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile	
	15 20 25 30	
	gac ctt cag ttt aag aaa acc cct cct aag atc cct tat aag gcc atc	264
	Asp Leu Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile	
	35 40 45	
15	gca ctt gcc act gtg ctg ttt ttg att ggc gcc ttt ctc att att ata	312
	Ala Leu Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile	
	50 55 60	
	ggc tcc ctc ctg ctg tca ggc tac atc agc aaa ggg ggg gca gcc cgg	360
	Gly Ser Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg	
20	65 70 75	
	gcc gtt cca gtg ctg atc att ggc att ctg gtg ttc cta ccc gga ttt	408
	Ala Val Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe	
	80 85 90	
	tac cac ctg cgc atc gct tac tat gca tcc aaa ggc tac cgt ggt tac	456
25	Tyr His Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr	
	95 100 105 110	
	tcc tat gat gac att cca gac ttt gat gac tagcaccac ccca	500
	Ser Tyr Asp Asp Ile Pro Asp Phe Asp Asp	
	115 120	
30	tagctgagga ggagtcacag tggaaactgtc ccagctttaa gatatctagc agaaactata	560
	gctgaggact aaggaattct gcagcttgca gatgtttaag aaaataatgg ccagattttt	620
	tgggtccttc ccaaagatgt taagtgaacc tacagtttagc taattaggac aagctctatt	680
	tttcateccct gggccctgac aagtttttcc acaggaatat gtatcatgga agaatagagg	740
	ttattctgta atggaaaagt gttgcctgcc accacccctct gtagagotga goattttttt	800
35	taaatagtct tcattgcca tttgttcttg tagcaaatgg aacaatgtgg tatggcta	860

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10 cctagaaata aaatgagtta acttc 1425

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&lt;210&gt; 61

&lt;211&gt; 307

&lt;212&gt; PRT

15 &lt;213&gt; Homo sapiens

&lt;400&gt; 61

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20 Pro Leu Ser Ala Ser Thr Asp Tyr Glu Gln Ser Thr Gly Met Gln Glu
20 25 30
Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln Leu Pro
35 40 45
25 Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe Ile Ser
50 55 60
Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr Pro Asn
65 70 75 80
Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe Ile Thr
85 90 95
30 Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr Cys Phe
100 105 110
Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr Asn Asn
115 120 125
35 Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln Thr Glu
130 135 140

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Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu Gly Ser  
 145 150 155 160  
 Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly Ala Gly  
 165 170 175  
 5 Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu Ser Gly  
 180 185 190  
 Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn Leu Ile  
 195 200 205  
 Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly Asp Asp  
 10 210 215 220  
 Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys Leu Tyr  
 225 230 235 240  
 Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val Lys Ser  
 245 250 255  
 15 Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu Tyr Glu  
 260 265 270  
 Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly Ala Phe  
 275 280 285  
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 20 290 295 300  
 Tyr Asp Val  
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 <210> 62  
 25 <211> 183  
 <212> PRT  
 <213> Homo sapiens  
 <400> 62  
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 1 5 10 15  
 Trp Ala Ile Glu Leu Ser Gly Pro Gly Gly Gly Ser Arg Gly Arg Ser  
 20 25 30  
 Asp Arg Gly Ser Gly Gln Gly Asp Ser Leu Tyr Pro Val Gly Tyr Leu  
 35 35 40 45

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      Asp Lys Gln Val Pro Asp Thr Ser Val Gln Glu Thr Asp Arg Ile Leu
      50              55              60
Val Glu Lys Arg Cys Trp Asp Ile Ala Leu Gly Pro Leu Lys Gln Ile
      65              70              75              80
5   Pro Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile
      85              90              95
Phe Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala
      100             105             110
Leu Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser Ser Ser Gln
10   115             120             125
Lys Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu
      130             135             140
Ala Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His
      145             150             155             160
15   Ala Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg Met Glu Phe
      165             170             175
Ser Gly Gly Gly Leu Leu Leu
      180

20   <210> 63
      <211> 327
      <212> PRT
      <213> Homo sapiens

25   <400> 63
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Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Ala Arg Pro Ser Ser Ala
      20              25              30
30   Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro Pro Leu Arg Glu
      35              40              45
Glu Ile Met Ala Asn Asn Phe Ser Leu Glu Ser His Asn Ile Ser Leu
      50              55              60
Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile Thr Leu Glu Arg
35   65              70              75              80

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Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr Ser Gly Asp Leu  
 85 90 95  
 Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu Gln Leu Glu Asn  
 100 105 110  
 5 Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr Thr Gln Tyr Arg  
 115 120 125  
 Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr Ser Cys Phe Phe  
 130 135 140  
 Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe Lys Val Pro Glu  
 10 145 150 155 160  
 Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val Gly Asp Ser Thr  
 165 170 175  
 Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu Asn Trp Thr Trp  
 180 185 190  
 15 Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly Val Gln Met Asn  
 195 200 205  
 Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr Lys Leu Lys Ile  
 210 215 220  
 Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp Cys Arg Ala Leu  
 20 225 230 235 240  
 Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu Val Val Leu Ser  
 245 250 255  
 Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val Ala Glu Val Ile  
 260 265 270  
 25 Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr Thr Gln Lys Lys  
 275 280 285  
 Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln Ile Glu Gln Leu  
 290 295 300  
 Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val Pro Arg His Arg  
 30 305 310 315 320  
 Lys Asn, Glu Ser Leu Gly Gln  
 325

&lt;210&gt; 64

35 &lt;211&gt; 223

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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 64

5 Met Lys Phe Val Pro Cys Leu Leu Leu Val Thr Leu Ser Cys Leu Gly  
     1                  5                  10                  15  
 Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Glu Glu  
                   20                  25                  30  
 Phe His Phe Gln Thr Gly Gly Arg Asp Ser Cys Thr Met Arg Pro Ser  
 10                  35                  40                  45  
 Ser Leu Gly Gln Gly Ala Gly Glu Val Trp Leu Arg Val Asp Cys Arg  
                   50                  55                  60  
 Asn Thr Asp Gln Thr Tyr Trp Cys Glu Tyr Arg Gly Gln Pro Ser Met  
                   65                  70                  75                  80  
 15 Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala Leu  
                   85                  90                  95  
 Gln Glu Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val Leu  
                   100                  105                  110  
 Arg Pro Ser Val Cys Arg Glu Ala Gly Pro Gln Ala His Met Gln Gln  
 20                  115                  120                  125  
 Val Thr Ser Ser Leu Lys Gly Ser Pro Glu Pro Asn Gln Gln Pro Glu  
                   130                  135                  140  
 Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr Glu  
                   145                  150                  155                  160  
 25 Ala Thr Gln Leu Gly Lys Asp Ser Met Glu Glu Leu Gly Lys Ala Lys  
                   165                  170                  175  
 Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg Pro  
                   180                  185                  190  
 Gly Gly Asn Glu Glu Ala Lys Lys Lys Ala Trp Glu His Cys Trp Lys  
 30                  195                  200                  205  
 Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly  
                   210                  215                  220

&lt;210&gt; 65

35 &lt;211&gt; 48

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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

5 Met Arg Leu Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg  
 1 5 10 15  
 Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys  
 20 25 30  
 Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser  
 10 35 40 45

&lt;210&gt; 66

&lt;211&gt; 371

&lt;212&gt; PRT

15 &lt;213&gt; Homo sapiens

&lt;400&gt; 66

Met Ala Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val  
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 20 Thr Gly Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met  
 20 25 30  
 Ala Glu Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe  
 35 40 45  
 Leu Gln Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala  
 25 50 55 60  
 Phe Tyr Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val  
 65 70 75 80  
 Asp Pro Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu  
 85 90 95  
 30 Cys Asp Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr  
 100 105 110  
 Ser Ala Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr  
 115 120 125  
 Gly Leu Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln  
 35 130 135 140

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Trp Leu Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu  
 145 150 155 160  
 Ala Asp Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val  
 165 170 175  
 5 Ile Thr Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile  
 180 185 190  
 Gln Met Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro  
 195 200 205  
 Leu Arg Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser  
 10 210 215 220  
 Leu Leu Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly  
 225 230 235 240  
 Asn Pro Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val  
 245 250 255  
 15 Gly Gln Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser  
 260 265 270  
 Ile Ala Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser  
 275 280 285  
 Ala Thr Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp  
 20 290 295 300  
 Ala Leu Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile  
 305 310 315 320  
 Leu Gly Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu  
 325 330 335  
 25 His Arg Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu  
 340 345 350  
 Glu Ser Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn  
 355 360 365  
 Asp Ala Ser  
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&lt;210&gt; 67

&lt;211&gt; 90

&lt;212&gt; PRT

35 &lt;213&gt; Homo sapiens

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<400> 67  
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 20 25 30  
 Gly Val Asp Gly Lys Glu Phe Pro Glu Val His Leu Gly Gln Trp Tyr  
 35 40 45  
 Phe Ile Ala Gly Ala Ala Pro Thr Lys Glu Glu Leu Ala Thr Phe Asp  
 10 50 55 60  
 Pro Val Asp Asn Ile Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met  
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 Gln Leu His Leu Arg Ala Thr Ile Arg Met  
 85 90  
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 <210> 68  
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 <212> PRT  
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 Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu  
 35 40 45  
 Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val  
 50 55 60  
 30 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe  
 65 70 75 80  
 Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile  
 85 90 95  
 Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg  
 35 100 105 110

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Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr  
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 Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Gly Arg Ala Lys Arg Leu  
 130 135 140  
 5 Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile  
 145 150 155 160  
 Thr Cys Thr Val Ile Phe Ile Val Trp Gly Val Leu Val His Leu Val  
 165 170 175  
 Ile Pro Pro Phe Val Phe Met Val Thr Glu Gly Trp Asn Tyr Ile Glu  
 10 180 185 190  
 Gly Leu Tyr Tyr Ser Phe Ile Thr Ile Ser Thr Ile Gly Phe Gly Asp  
 195 200 205  
 Phe Val Ala Gly Val Asn Pro Ser Ala Asn Tyr His Ala Leu Tyr Arg  
 210 215 220  
 15 Tyr Phe Val Glu Leu Trp Ile Tyr Leu Gly Leu Ala Trp Leu Ser Leu  
 225 230 235 240  
 Phe Val Asn Trp Lys Val Ser Met Phe Val Glu Val His Lys Ala Ile  
 245 250 255  
 Lys Lys Arg Arg Arg Arg Arg Lys Glu Ser Phe Glu Ser Ser Pro His  
 20 260 265 270  
 Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val  
 275 280 285  
 Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu  
 290 295 300  
 25 Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu  
 305 310 315 320  
 Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala  
 325 330 335  
 Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val  
 30 340 345 350  
 Pro Thr Leu Glu Glu Val Ser Gln Thr Leu Arg Ser Lys Gly His Val  
 355 360 365  
 Ser Arg Ser Pro Asp Glu Glu Ala Val Ala Arg Ala Pro Glu Asp Ser  
 370 375 380  
 35 Ser Pro Ala Pro Glu Val Phe Met Asn Gln Leu Asp Arg Ile Ser Glu



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385                      390                      395                      400  
 Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln  
                                  405                      410                      415  
 Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu  
 5                                   420                      425                      430  
 Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser  
                                  435                      440                      445  
 Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe  
                                  450                      455                      460  
 10 Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser  
                                  465                      470                      475                      480  
 Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro  
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 Lys Gly Thr  
 15  
  
 <210> 69  
 <211> 106  
 <212> PRT  
 20 <213> Homo sapiens  
  
 <400> 69  
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                                  20                      25                      30  
 Glu Gln Leu His Ser Met Arg Gln Ala Glu Leu Ala Gln Trp Gln Lys  
                                  35                      40                      45  
 Val Leu Pro Arg Arg Arg Thr Arg Asn Ile Val Thr Gly Leu Gly Ile  
 30                                   50                      55                      60  
 Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr Thr Phe Tyr Ser Ile Ser  
                                  65                      70                      75                      80  
 Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp Glu Ala Lys Ala Ala Arg  
                                  85                      90                      95  
 35 Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser

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100

105

<210> 70  
 <211> 152  
 5 <212> PRT  
 <213> Homo sapiens  
  
 <400> 70  
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 Ala Gln Lys Gly Lys Ser Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile  
 35 40 45  
 15 Ser Leu Phe Leu Ile Ile Ser Met Cys Leu Leu Phe Leu Trp Lys Lys  
 50 55 60  
 Tyr Gln Pro Tyr Lys Val Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu  
 65 70 75 80  
 Thr Glu Tyr Arg Lys Ala Gln Thr Phe Ser Gly His Glu Asp Ala Leu  
 20 85 90 95  
 Asp Asp Phe Gly Ile Tyr Glu Phe Val Ala Phe Pro Asp Val Ser Gly  
 100 105 110  
 Val Ser Arg Ile Pro Ser Arg Ser Val Pro Ala Ser Asp Cys Val Ser  
 115 120 125  
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 130 135 140  
 Ala Gln Gln Gln Asp His Pro Glu  
 145 150  
  
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 <212> DNA  
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 35 <400> 71

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 aattttatta gctctctggg agtgagctac atgatgttgt gcactgaaaa ttaccacaat 240  
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 atgaagacaa atactgtgt cagaccatac tgtttcattg aatttgataa cttcattcag 360  
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 15 tttcatgtga ctgtgggagc atttgttaca ctacagatct ggctaaggca agcccaaggc 900  
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&lt;210&gt; 72

&lt;211&gt; 549

20 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 72

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 tcgctctacc cagtcgggta cttggacaag caagtgcctg ataccagcgt gcaagagaca 180  
 gaccggatcc tgggtggagaa gcgctgctgg gacatcgctt tgggtccctt caaacagatt 240  
 cccatgaata tcttcatcat gtacatggca ggcaatacta tctccatctt ccttactatg 300  
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 ctgatgggtt tggcattggc tgtttacaag tgccagtcca tgggactgtt acctacacat 480  
 gcacgggatt ggttagcctt cattgagccc cctgagagaa tggagtacag tgggtggagg 540  
 ctgcttttg 549

35 &lt;210&gt; 73

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&lt;211&gt; 981

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

5 &lt;400&gt; 73

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cagtgccttc	tcgctgcgcg	gcgcaccaagc	tcggcggacg	gcagtgcctc	agattcgcc	120
tttacaagtc	cacctctcag	agaagaaata	atggcaata	acttttctt	ggagagtc	180
aacatatac	tgactgaaca	ttctagtatg	ccagtagaaa	aaaatatcac	tttagaagg	240
ccttctaag	taaatctcac	atgccagttc	acaacatctg	gggatttgaa	tgcaagaa	300
gtgacttgga	aaaaagatgg	tgaacaactt	gagaataatt	atcttgtcag	tgcaacagga	360
agcaccttgt	atacccaata	caggttcacc	atcattaata	gcaaacaaat	gggaagttat	420
tcttgtttct	ttcgagagga	aaaggaacaa	aggggaacat	ttaatttcaa	agtcctgaa	480
cttcattgga	aaaacaagcc	attgatctct	tacgtagggg	attctactgt	cttgacatgt	540
aatgtcaaa	attgttttcc	tttaaatggg	acctgggtaca	gtagtaattg	gagtgtaaag	600
gttcctgttg	gtgttcaaat	gaataaatat	gtgatcaatg	gaacatatgc	taacgaacaa	660
aagctgaaga	taacacaact	tttggaggaa	gatggggaat	cttactgggtg	ccgtgcaacta	720
ttccaattag	gcgagagtga	agaacacatt	gagcttgtgg	tgetgagcta	tttgggtccc	780
ctcaaaccat	ttcttgtaat	agtggctgag	gtgattcttt	tagtggccac	cattctgctt	840
tgtgaaaagt	acacacaaaa	gaaaaagaag	cactcagatg	aggggaaaga	atttgagcag	900
attgaacagc	tgaatcaga	tgatagcaat	ggtagagaaa	ataatgtccc	caggcataga	960
aaaaatgagt	ctctgggcca	g				981

&lt;210&gt; 74

25 &lt;211&gt; 669

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 74

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	tatggcaatg tggctcccaa gaccccccgc ggtcgctct tctgtgtttt ctatggtctc	360
	ttcgggggtg cgtctctgct gacgtggatc agtgccctgg gcaagttctt cgggggacgt	420
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&lt;210&gt; 79

&lt;211&gt; 318

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&lt;213&gt; Homo sapiens

&lt;400&gt; 79

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35

80/177

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 gttccagcct ctgatttgtt atcggggcaa gatttgaca gtacagtga tgaagttatt 420  
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 Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp  
 1 5 10  
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 15 20 25 30  
 cag gag tgc aga aag tat ttt aaa atg ctt tgc agg aaa ctt gct caa 203  
 Gln Glu Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln  
 35 40 45  
 30 ctt cct gat aga tgt aca ctg aaa act gga cat tat aac att aat ttt 251  
 Leu Pro Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe  
 50 55 60  
 att agc tct ctg gga gtg agc tac atg atg ttg tgc act gaa aat tac 299  
 Ile Ser Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr  
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	Pro Asn Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe	
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	95 100 105 110	
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	Cys Phe Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr	
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	Asn Asn Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln	
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	acg gaa atc aag ctg agg cct cct tat caa att tcc atg tgc gaa ctg	539
	Thr Glu Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu	
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	ggg tca gcc aat gga gtc aca tca gca ttt tct gtt gac tgt aaa ggt	587
	Gly Ser Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly	
	160 165 170	
	gct ggt aag att tct tct gct cac cag cga ctg gaa cca gca act ctg	635
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	tca ggg att gta gga ttt atc ctt agt ctt tta tgt gga gct ctg aat	683
	Ser Gly Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn	
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25	tta att cga ggc ttt cat gct ata gaa agt ctc ctg cag agt gat ggt	731
	Leu Ile Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly	
	210 215 220	
	gat gat ttt aat tac atc att gca ttt ttc ctt gga aca gca gcc tgc	779
	Asp Asp Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys	
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	ctt lac cag tgt tat tta ctt gtc tac tac acc ggc tgg cgg aat gtc	827
	Leu Tyr Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val	
	240 245 250	
	aaa tct ttt ttg act ttt ggc tta atc tgt cta tgc aac atg tat ctc	875
35	Lys Ser Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu	

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                          290                      295                      300  
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 Pro Asp Tyr Asp Val  
 10                      305  
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 aggagaagct ctgctttctt tctctccaac ttctctttt taaaatcagc atgatgtgcc      1140  
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 30    Met Thr Ala Gln Gly Gly Leu Val  
    1    5  
 gct aac cga ggc cgg cgc ttc aag tgg gcc att gag cta agc ggg cct      158  
 Ala Asn Arg Gly Arg Arg Phe Lys Trp Ala Ile Glu Leu Ser Gly Pro  
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 35    gga gga ggc agc agg ggt cga agt gac cgg ggc agt ggc cag gga gac      206

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	Ser Leu Tyr Pro Val Gly Tyr Leu Asp Lys Gln Val Pro Asp Thr Ser	
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	Val Gln Glu Thr Asp Arg Ile Leu Val Glu Lys Arg Cys Trp Asp Ile	
	60 65 70	
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10	Ala Leu Gly Pro Leu Lys Gln Ile Pro Met Asn Leu Phe Ile Met Tyr	
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	atg gca ggc aac act atc tcc atc ttc cct act atg atg gtg tgt atg	398
	Met Ala Gly Asn Thr Ile Ser Ile Phe Pro Thr Met Met Val Cys Met	
	90 95 100	
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	Met Ala Trp Arg Pro Ile Gln Ala Leu Met Ala Ile Ser Ala Thr Phe	
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	Lys Met Leu Glu Ser Ser Ser Gln Lys Phe Leu Gln Gly Leu Val Tyr	
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	ctc att ggg aac ctg atg ggt ttg gca ttg gct gtt tac aag tgc cag	542
	Leu Ile Gly Asn Leu Met Gly Leu Ala Leu Ala Val Tyr Lys Cys Gln	
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	tcc atg gga ctg tta cct aca cat gca tgc gat tgg tta gcc ttc att	590
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	gag ccc cct gag aga atg gag ttc agt ggt gga gga ctg ctt ttg tgaac	640
	Glu Pro Pro Glu Arg Met Glu Phe Ser Gly Gly Gly Leu Leu Leu	
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84/177

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    acctcttgcc gcc atg cgc gcc ctc ccc gcc ctg ctg gag gcc agg gcg    169
                Met Arg Ala Leu Pro Gly Leu Leu Glu Ala Arg Ala
15                1                5                10
    cgt acg ccc cgg ctg ctc ctc ctc cag tgc ctt ctc gct gcc gcg cgc    217
    Arg Thr Pro Arg Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Ala Arg
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    cca agc tcg gcg gac gcc agt gcc cca gat tcg cct ttt aca agt cca    265
20  Pro Ser Ser Ala Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro
                30                35                40
    cct ctc aga gaa gaa ata atg gca aat aac ttt tcc ttg gag agt cat    313
    Pro Leu Arg Glu Glu Ile Met Ala Asn Asn Phe Ser Leu Glu Ser His
                45                50                55                60
25  aac ata tca ctg act gaa cat tct agt atg cca gta gaa aaa aat atc    361
    Asn Ile Ser Leu Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile
                65                70                75
    act tta gaa agg cct tct aat gta aat ctc aca tgc cag ttc aca aca    409
    Thr Leu Glu Arg Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr
30                80                85                90
    tct ggg gat ttg aat gca gta aat gtg act tgg aaa aaa gat ggt gaa    457
    Ser Gly Asp Leu Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu
                95                100                105
    caa ctt gag aat aat tat ctt gtc agt gca aca gga agc acc ttg tat    505
35  Gln Leu Glu Asn Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr

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5	tct tgt ttc ttt cga gag gaa aag gaa caa agg gga aca ttt aat ttc			601
	Ser Cys Phe Phe Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe			
	145	150	155	
	aaa gtc cct gaa ctt cat ggg aaa aac aag cca ttg atc tct tac gta			649
	Lys Val Pro Glu Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val			
10	160	165	170	
	ggg gat tct act gtc ttg aca tgt aaa tgt caa aat tgt ttt cct tta			697
	Gly Asp Ser Thr Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu			
	175	180	185	
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15	Asn Trp Thr Trp Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly			
	190	195	200	
	gtt caa atg aat aaa tat gtg atc aat gga aca tat gct aac gaa aca			793
	Val Gln Met Asn Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr			
	205	210	215	220
20	aag ctg aag ata aca caa ctt ttg gag gaa gat ggg gaa tct tac tgg			841
	Lys Leu Lys Ile Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp			
	225	230	235	
	tgc cgt gca cta ttc caa tta ggc gag agt gaa gaa cac att gag ctt			889
	Cys Arg Ala Leu Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu			
25	240	245	250	
	gtg gtg ctg agc tat ttg gtg ccc etc aaa cca ttt ctt gta ata gtg			937
	Val Val Leu Ser Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val			
	255	260	265	
	gct gag gtg att ctt tta gtg gcc acc att ctg ctt tgt gaa aag tac			985
30	Ala Glu Val Ile Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr			
	270	275	280	
	aca caa aag aaa aag aag cac tca gat gag ggg aaa gaa ttt gag cag			1033
	Thr Gln Lys Lys Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln			
	285	290	295	300
35	att gaa cag ctg aaa tca gat gat agc aat ggt ata gaa aat aat gtc			1081

Ile Glu Gln Leu Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val

315

1130

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325

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1250

1310

1370

1430

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1550

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1730

1753

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106

30

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1

154

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20

25

30

202

87/177

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5	cgc aac aca gac cag acc tac tgg tgt gag tac agg ggg cag ccc agc	298		
	Arg Asn Thr Asp Gln Thr Tyr Trp Cys Glu Tyr Arg Gly Gln Pro Ser			
	65	70	75	
	atg tgc cag gct ttc gct gct gac ccc aaa tct tac tgg aat caa gcc	346		
	Met Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala			
10	80	85	90	95
	ctg cag gag ctg agg cgc ctt cac cat gcg tgc cag ggg gcc ccg gtg	394		
	Leu Gln Glu Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val			
	100	105	110	
	ctt agg cca tcc gtg tgc agg gag gct gga ccc cag gcc cat atg cag	442		
15	Leu Arg Pro Ser Val Cys Arg Glu Ala Gly Pro Gln Ala His Met Gln			
	115	120	125	
	cag gtg act tcc agc ctc aag ggc agc cca gag ccc aac cag cag cct	490		
	Gln Val Thr Ser Ser Leu Lys Gly Ser Pro Glu Pro Asn Gln Gln Pro			
	130	135	140	
20	gag gct ggg acg cca tct ctg agg ccc aag gcc aca gtg aaa ctc aca	538		
	Glu Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr			
	145	150	155	
	gaa gca aca cag ctg gga aag gac tcg atg gaa gag ctg gga aaa gcc	586		
	Glu Ala Thr Gln Leu Gly Lys Asp Ser Met Glu Glu Leu Gly Lys Ala			
25	160	165	170	175
	aaa ccc acc acc cga ccc aca gcc aaa cct acc cag cct gga ccc agg	634		
	Lys Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg			
	180	185	190	
	ccc gga ggg aat gag gaa gca aag aag aag gcc tgg gaa cat tgt tgg	682		
30	Pro Gly Gly Asn Glu Glu Ala Lys Lys Lys Ala Trp Glu His Cys Trp			
	195	200	205	
	aaa ccc ttc cag gcc ctg tgc gcc ttt ctc atc agc ttc ttc cga ggg	730		
	Lys Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly			
	210	215	220	
35	tgacagggtga aagacccta cagatctgac ctctccctga cagacaacca tctcttttta	790		

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tattatgccg ctttcaatcc aacgttctca cactggaaga agagagtctc taatcagatg 850  
 caacggccca aattcttgat ctgcagcttc tctgaagttt ggaaaagaaa ctttccttcc 910  
 tggagtgtgc agagtccagc aatatgatag ggaacagggtg ctgatggggc caagagtgcac 970  
 aagcatacac aactaactat tatctgtaga agttttgott tgttgatctg agccttctat 1030  
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 Met Arg Leu Leu  
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 Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Glu Ala Ser  
 5 10 15 20  
 gcc aat ctg gcc gcc gtg ccc agc aag aga tta aag atg cag tac gcc 150  
 Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala

25 25 30 35  
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 Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser  
 40 45

30 gttataggcg ggtgtttgag gactacatgc gggttattag ccagcgggtac ccagacatcc 250  
 gcattgaagg agagaattac ctccctcaac caatatatag acacatagca tctttcctgt 310  
 cagtcttcaa actagtatta ataggcttaa taattgttgg caaggatcct tttgctttct 370  
 ttggcatgca agctcctagc atctggcagt ggggccaaga aaataaggtt tatgcatgta 430  
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 agataacttt aatgatgta cctgtgtggt ctaagctgga atctggtcac cttccatcca 550  
 35 tgcaacaact tgttcaaatt cttgacaatg aatgaagct caatgtgcct atggattcaa 610



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	tccccaccca	tccatcatag	caccacctat	cagcaactgaa	aactcttttg	cattaaggga	670
	tcattgcaag	agcagcgtga	ctgacattat	gaaggcctgt	actgaagaca	gcaagctgtt	730
	agtacagacc	agatgcttcc	ttggcaggct	cgttgtacct	cttggaaaac	ctcaatgcaa	790
	gatagtgttt	cagtgtggc	atattttgga	attctgcaca	ttcatggagt	gcaataatac	850
5	tgtatagctt	tccccacctc	ccacaaaatc	acccagttaa	tgtgtgtgtg	tgtttttttt	910
	tttaaggtaa	acattactac	ttgtaacttt	ttttcttagt	catatttgaa	aaagtagaaa	970
	attgagttac	aatttgattt	ttttccaaa	gatgtctgtt	aaatctgttg	tgtttttata	1030
	tgaatatttg	ttttttatag	tttaaaattg	atcctttggg	aatccagttg	aagtccccaa	1090
	atactttata	agagtttctc	agacatctct	aatttggcca	tgtccagttt	atacagttta	1150
10	caaatatag	cagatgcaag	attatggggg	aaatcctata	ttcagagtac	tctataaatt	1210
	tttgtgtatg	tgtgtatgtg	cgtgtgatta	ccagagaact	actaaaaaaa	ccaaactggt	1270
	tttaaatcct	attgtgtagt	taaagtgtca	tgccttgacc	aatctaata	attgattaat	1330
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	1						
	tgg acc aag tac	cag ctg ttc	ctg gcc ggg	ctc atg ctt	gtt acc ggc		104
	Trp Thr Lys Tyr	Gln Leu Phe	Leu Ala Gly	Leu Met Leu	Val Thr Gly		
	5	10	15				
30	tcc atc aac acg	ctc tcg gca	aaa tgg gcg	gac aat ttc	atg gcc gag		152
	Ser Ile Asn Thr	Leu Ser Ala	Lys Trp Ala	Asp Asn Phe	Met Ala Glu		
	20	25	30				
	ggc tgt gga ggg	agc aag gag	cac agc ttc	cag cat ccc	ttc ctc cag		200
	Gly Cys Gly Gly	Ser Lys Glu	His Ser Phe	Gln His Pro	Phe Leu Gln		
35	35	40	45	50			

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	gca gtg ggc atg ttc ctg gga gaa ttc tcc tgc ctg gct gcc ttc tac	248
	Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala Phe Tyr	
	55 60 65	
	ctc ctc cga tgc aga gct gca ggg caa tca gac tcc agc gta gac ccc	296
5	Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val Asp Pro	
	70 75 80	
	cag cag ccc ttc aac cct ctt ctt ttc ctg ccc cca gcg ctc tgt gac	344
	Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu Cys Asp	
	85 90 95	
10	atg aca ggg acc agc ctc atg tat gtg gct ctg aac atg acc agt gcc	392
	Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr Ser Ala	
	100 105 110	
	tcc agc ttc cag atg ctg cgg ggt gca gtg atc ata ttc act ggc ctg	440
	Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr Gly Leu	
15	115 120 125 130	
	ttc tgc gtg gcc ttc ctg ggc cgg agg ctg gtg ctg agc cag tgg ctg	488
	Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln Trp Leu	
	135 140 145	
	ggc atc cta gcc acc atc gcg ggg ctg gtg gtc gtg ggc ctg gct gac	536
20	Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu Ala Asp	
	150 155 160	
	ctc ctg agc aag cac gac agt cag cac aag ctc agc gaa gtg atc aca	584
	Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val Ile Thr	
	165 170 175	
25	ggg gac ctg ttg atc atc atg gcc cag atc atc gtt gcc atc cag atg	632
	Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile Gln Met	
	180 185 190	
	gtg cta gag gag aag ttc gtc tac aaa cac aat gtg cac cca ctg cgg	680
	Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro Leu Arg	
30	195 200 205 210	
	gca gtt ggc act gag ggc ctc ttt ggc ttt gtg atc ctc tcc ctg ctg	728
	Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser Leu Leu	
	215 220 225	
	ctg gtg ccc atg tac tac atc ccc gcc ggc tcc ttc agc gga aac cct	776
35	Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly Asn Pro	

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	230	235	240	
	cgt ggg aca ctg gag gat gca ttg gac gcc ttc tgc cag gtg ggc cag			824
	Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val Gly Gln			
	245	250	255	
5	cag ccg ctc att gcc gtg gca ctg ctg ggc aac atc agc agc att gcc			872
	Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser Ile Ala			
	260	265	270	
	ttc ttc aac ttc gca ggc atc agc gtc acc aag gaa ctg agc gcc acc			920
	Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser Ala Thr			
10	275	280	285	290
	acc cgc atg gtg ttg gac agc ttg cgc acc gtt gtc atc tgg gca ctg			968
	Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp Ala Leu			
	295	300	305	
	agc ctg gca ctg ggc tgg gag gcc ttc cat gca ctg cag atc ctt ggc			1016
15	Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile Leu Gly			
	310	315	320	
	ttc ctc ata ctc ctt ata ggc act gcc ctc taa aat ggg ota oao cgt			1064
	Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu His Arg			
	325	330	335	
20	ccg ctg ctg ggc cgc ctg tcc agg ggc cgg ccc ctg gca gag gag agc			1112
	Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu Glu Ser			
	340	345	350	
	gag cag gag aga ctg ctg ggt ggc acc cgc act ooc atc aat gat gcc			1160
	Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn Asp Ala			
25	355	360	365	370
	agc tgagggtccc tggaggettc taatgccacc cgggtgetcc ttctccc			1210
	Ser			
	tgagactgag gccacacagg ctggtgggcc ccgaatgcc tatecccaag gctcaccct			1270
30	gtccctccc tgcagaaccc ccagggcagc tgetgccaca gaagataaca acacccaagt			1330
	cctcttttc tcaactaccac ctgcagggtg gtgttaccca gccccacaa gctgagtg			1390
	agtggcagac ctcagctctc tggacccctc ctacagcact agagctaat catgaagtg			1450
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	Met Phe His Gln Ile	
	1 5	
	t g g g a g c t c t g c t c t a c t t c t a t g g t a t t a t c e t t a a c t c c a t c t a c	102
	Trp Ala Ala Leu Leu Tyr Phe Tyr Gly Ile Ile Leu Asn Ser Ile Tyr	
	10 15 20	
15	c a g t g c c c t g a g c a c a g t c a a c t g a c a c t c t g g g c g t g a t g g g a a g	150
	Gln Cys Pro Glu His Ser Gln Leu Thr Thr Leu Gly Val Asp Gly Lys	
	25 30 35	
	g a g t t c c c a g a g g t c c a c t t g g g c a g t g g t a c t t t a t c g c a g g g c a	198
	Glu Phe Pro Glu Val His Leu Gly Gln Trp Tyr Phe Ile Ala Gly Ala	
20	40 45 50	
	g c t c c c a c c a a g g a g g a g t t g g c a a c t t t g a c c c t g t g a c a a c a t t	246
	Ala Pro Thr Lys Glu Glu Leu Ala Thr Phe Asp Pro Val Asp Asn Ile	
	55 60 65	
25	g t c t t c a a t a t g g c t g c t g g c t c t g c c c g a t g c a g c t c c a c e t t c g t	294
	Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met Gln Leu His Leu Arg	
	70 75 80 85	
	g c t a c c a t c c g c a t g t g a g t g g a a g a t g g g g c t c t g t g t g c c c c g g	340
	Ala Thr Ile Arg Met	
	90	
30	a a a t g g a t c t a c c a c c c t g a c t g a a g g g a g c a c a g a t c t c a g a a c t g a a g g c c g c c c t g a c	400
	a t g a a g a c t g a g c t c t t t t c c a g c t c a t g c c a g g t g g a a t c a t g c t g a a t g a c a c a g g c	460
	c a g g g t t a c c a g c g c t t t t c t c c t c a c a a t c g t c c a c c a c a t c c t c c c g a a a a g t g t g t g	520
	g a g g a a t t c a a g t c c c t g a c t t c c t g c c t g g a c t c c a a a g c c t t c t t a t t g a c t c c t a g g	580
	a a t c a a g a g g c c t g t g a g c t g t c c a a t a a c t g a c c t g t a a c t t c a t c t a a g t c c c a g a t	640
35	g g g t a c a a t g g g a g c t g a g t t g t t g g a g g g a a a g c t g g a g a c t t c c a g c t c c a g e t c c c	700

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	tgggtgttcgc ccaccccggg ccgcgtgagt ggggccccac gcagtcctcc gcactccgtg	180
15	ggccaacttg gccaaagcaac tctgtccggg gacgggtgct tgcggggggg gagtacggg	240
	cactgcgcgt cgcggagctc aaattcaaac agctgttttc agaggtctga gggcgggcgg	300
	actggtagca gctggggcta ggagaggctt tctctaggag ggggcgcctc gggagcc	357
20		
	atg gtg gac cgg ggc cct ctg etc acc tgg gcc atc atc ttc tac ctg	405
	Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu	
	1 5 10 15	
	gcc atc ggg gcg gcg atc ttc gaa gtg ctg gag gag cca cac tgg aag	453
	Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys	
25	20 25 30	
	gag gcc aag aaa aac tac tac aca cag aag ctg cat ctg etc aag gag	501
	Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu	
	35 40 45	
	ttc ccg tgc ctg ggt cag gag gcc ctg gac aag atc cta gag gtg gta	549
30	Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val	
	50 55 60	
	tct gat get gca gga cag ggt gtg gcc atc aca ggg aac cag acc ttc	597
	Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe	
	65 70 75 80	
35	aac aac tgg aac tgg ccc aat gca atg att ttt gca gcg acc gtc att	645

	Asn	Asn	Trp	Asn	Trp	Pro	Asn	Ala	Met	Ile	Phe	Ala	Ala	Thr	Val	Ile	
				85						90					95		
	acc	acc	att	gga	tat	ggc	aat	gtg	gct	ccc	aag	acc	ccc	gcc	ggt	cgc	693
	Thr	Thr	Ile	Gly	Tyr	Gly	Asn	Val	Ala	Pro	Lys	Thr	Pro	Ala	Gly	Arg	
5				100					105					110			
	etc	ttc	tgt	gtt	ttc	tat	ggt	ctc	ttc	ggg	gtg	cgg	ctc	tgc	ctg	acg	741
	Leu	Phe	Cys	Val	Phe	Tyr	Gly	Leu	Phe	Gly	Val	Pro	Leu	Cys	Leu	Thr	
				115					120					125			
	tgg	atc	agt	gcc	ctg	ggc	aag	ttc	ttc	ggg	gga	cgt	gcc	aag	aga	cta	789
10	Trp	Ile	Ser	Ala	Leu	Gly	Lys	Phe	Phe	Gly	Gly	Arg	Ala	Lys	Arg	Leu	
				130					135					140			
	ggg	cag	ttc	ctt	acc	aag	aga	ggg	gtg	agt	ctg	cgg	aag	gcg	cag	atc	837
	Gly	Gln	Phe	Leu	Thr	Lys	Arg	Gly	Val	Ser	Leu	Arg	Lys	Ala	Gln	Ile	
				145					150					155		160	
15	acg	tgc	aca	gtc	atc	ttc	atc	gtg	tgg	ggc	gtc	cta	gtc	cac	ctg	gtg	885
	Thr	Cys	Thr	Val	Ile	Phe	Ile	Val	Trp	Gly	Val	Leu	Val	His	Leu	Val	
				165					170					175			
	atc	cca	ccc	ttc	gta	ttc	atg	gtg	act	gag	ggg	tgg	aac	tac	atc	gag	933
	Ile	Pro	Pro	Phe	Val	Phe	Met	Val	Thr	Glu	Gly	Trp	Asn	Tyr	Ile	Glu	
20				180					185					190			
	ggc	ctc	tac	tac	tcg	ttc	atc	acc	atc	tcg	acc	atc	ggc	ttc	ggt	gac	981
	Gly	Leu	Tyr	Tyr	Ser	Phe	Ile	Thr	Ile	Ser	Thr	Ile	Gly	Phe	Gly	Asp	
				195					200					205			
	ttt	gtg	gcc	ggt	gtg	aac	ccc	agc	gcc	aac	tac	cac	gcc	ctg	tac	cgc	1029
25	Phe	Val	Ala	Gly	Val	Asn	Pro	Ser	Ala	Asn	Tyr	His	Ala	Leu	Tyr	Arg	
				210					215					220			
	tac	ttc	gtg	gag	ctc	tgg	atc	tac	ttg	ggg	ctg	gcc	tgg	ctg	tcg	ctt	1077
	Tyr	Phe	Val	Glu	Leu	Trp	Ile	Tyr	Leu	Gly	Leu	Ala	Trp	Leu	Ser	Leu	
				225					230					235		240	
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	Phe	Val	Asn	Trp	Lys	Val	Ser	Met	Phe	Val	Glu	Val	His	Lys	Ala	Ile	
				245					250					255			
	aag	aag	cgg	cgg	cgg	cga	cgg	aag	gag	tcg	ttt	gag	agc	tcg	cca	cac	1173
	Lys	Lys	Arg	Arg	Arg	Arg	Arg	Lys	Glu	Ser	Phe	Glu	Ser	Ser	Pro	His	
35				260					265					270			

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	tcc cgg aag gcc ctg cag gtg aag ggg agc aca gcc tcc aag gac gtc	1221
	Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val	
	275 280 285	
	aac atc ttc agc ttt ctt tcc aag aag gaa gag acc tac aac gac ctc	1269
5	Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu	
	290 295 300	
	atc aag cag atc ggg aag aag gcc atg aag aca agc ggg ggt ggg gag	1317
	Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu	
	305 310 315 320	
10	acg ggc ccg ggc cca ggg ctg ggg cct caa ggc ggt ggg ctc cca gca	1365
	Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala	
	325 330 335	
	ctg ccc cct tcc ctg gtg ccc ctg gta gtc tac tcc aag aac cgg gtg	1413
	Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val	
15	340 345 350	
	ccc acc ttg gaa gag gtg tca cag aca ctg agg agc aaa ggc cac gta	1461
	Pro Thr Leu Glu Glu Val Ser Gln Thr Leu Arg Ser Lys Gly His Val	
	355 360 365	
	tca agg tcc cca gat gag gag gct gtg gca cgg gcc cct gaa gac agc	1509
20	Ser Arg Ser Pro Asp Glu Glu Ala Val Ala Arg Ala Pro Glu Asp Ser	
	370 375 380	
	tcc cct gcc ccc gag gtg ttc atg aac cag ctg gac cgc atc agc gag	1557
	Ser Pro Ala Pro Glu Val Phe Met Asn Gln Leu Asp Arg Ile Ser Glu	
	385 390 395 400	
25	gaa tgc gag cca tgg gac gcc cag gac tac cac cca ctc atc ttc cag	1605
	Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln	
	405 410 415	
	gac gcc agc atc acc ttc gtg aac acg gag gct ggc ctc tca gac gag	1653
	Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu	
30	420 425 430	
	gag acc tcc aag tcc tcg cta gag gac aac ttg gca ggg gag gag agc	1701
	Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser	
	435 440 445	
	ccc cag cag ggg gct gaa gcc aag gcg ccc ctg aac atg ggc gag ttc	1749
35	Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe	

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	450	455	460	
	ccc tcc tcc tcc gag tcc acc ttc acc agc act gag tct gag ctc tct	1797		
	Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser			
	465	470	475	480
5	gtg cct tac gaa cag ctg atg aat gag tac aac aag gct aac agc ccc	1845		
	Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro			
	485	490	495	
	aag ggc aca tgaggcaggg cagggtccccc accccacatt tgatgg	1890		
	Lys Gly Thr			
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	attactgagc tggcatttg gagaggagc tctgaagtgt ctggggaggt accgtgtgc	2310		
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	ctgtgtctt ctccttccct gtgccctgaa caaggacctc actgccgcc ttccctccc	2850		
	accagccccc ttgggcccag cagggtgagg ccaaatgtct cttggccca aaatgggtga	2910		
	tggtcagata tgtgaatcaa gctcctttct ctagctagtg tttgatgtgc acgtgtgtgt	2970		
	gcacagtgcg tgtgtgcaca cgcacacctg tgcactcgtg tgtgtttaag aaaggaaagg	3030		
30	atttgggctg gggagcaaaa gataatgtga aactgttggg ggactctctg gtgaggggtg	3090		
	ggcagaactt gctgctaacta gattcttggg gttctccatg atgttcaccc tggggctggc	3150		
	ccactgtgtc ctgaatgttt ttgtatttt ttgtttatt ttttaaaaa actgctgttt	3210		
	ttatataact ggaatctgtt gttggcttca gacacagtgg ttaagagca ggggtcccaag	3270		
	gattgggaga tctagtgtct gccctcctgc cctgcaactc aattgggctt ttttcggtga	3330		
35	cctcatccaa ggccatgatg tcaagggcc agtccccaag cagaggtgga gaaggggaca	3390		



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ctgaggtgag caaaagcagg aaggggcac cactgcgggt gactggaggc cgggcaggaa 3450  
 gcaagtcac agagccgctc agctccgttc actctctgcc ttctgcccc ctactgtggg 3510  
 gcagtggggc cagagcccac ctccccaaca tgtgaagaca gtgatgggca cgtgccaca 3570  
 cccccaette tctagccgtt tgcagaggcc gccaccacgc aggggcctga aaaggagcag 3630  
 5 cctcgtatct ttctgtgaaa tgttttaatg aacctgttg ttgctgggtg tcttggcacc 3690  
 gcgcacactg tatgtacata ctggcaacga tgtcaaatgt aatttatctt aacattttta 3750  
 caataaaca tgaggtgg 3768

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 10 <211> 770  
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 <213> Homo sapiens  
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 15 <222> (24)...(344)

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 gat tct aag cgt gga gag gcc ccg ttc gct cag cgt atc gac ccg act 101  
 Asp Ser Lys Arg Gly Glu Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr  
 15 20 25  
 cgg gag aag ctg aca ccc gag caa ctg cat tcc atg cgg cag gcg gag 149  
 25 Arg Glu Lys Leu Thr Pro Glu Gln Leu His Ser Met Arg Gln Ala Glu  
 30 35 40  
 ctt gcc cag tgg cag aag gtc cta cca cgg cgg cga acc cgg aac atc 197  
 Leu Ala Gln Trp Gln Lys Val Leu Pro Arg Arg Arg Thr Arg Asn Ile  
 45 50 55  
 30 gtg acc ggc cta gcc atc ggg gcc ctg gtg ttg gct att tat ggt tac 245  
 Val Thr Gly Leu Gly Ile Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr  
 60 65 70  
 acc ttc tac tcg att tcc cag gag cgt ttc cta gat gag cta gaa gac 293  
 Thr Phe Tyr Ser Ile Ser Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp  
 35 75 80 85 90

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gag gcc aaa gct gcc cga gcc cga gct ctg gca agg gcg tca ggg tcc 341  
 Glu Ala Lys Ala Ala Arg Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser  
 95 100 105  
 taatctgga tgggtattga tcatgtccaa cctgctggag ccccttcaca tggtagatga 400  
 5 tgccecatga cctgtagaa attgaatcct gtcacaaaca ttgtggcct tottactaac 460  
 cttggaccgt gattgagccc aagaaaccag ggacttacgc atttggccaa tgcacaaaga 520  
 acagaacttt gcccaactgca cacttgctgt gtacaatgac tgagcccttt cttgtagttt 580  
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 gggttaccct cttcaacttc cagggacgca gttgttacga ggtagacgt ggcagctctg 700  
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 Met Asp Tyr Val Cys Cys  
 25 1 5  
 gct tac aac aac ata acc gcc agg caa gat gaa act cat ttc aca gtt 161  
 Ala Tyr Asn Asn Ile Thr Gly Arg Gln Asp Glu Thr His Phe Thr Val  
 10 15 20  
 atc atc act tcc gta gga ctg gag aag ctt gca cag aaa gga aaa tca 209  
 30 Ile Ile Thr Ser Val Gly Leu Glu Lys Leu Ala Gln Lys Gly Lys Ser  
 25 30 35  
 ttg tca cct tta gca agt ata act gga ata tca cta ttt ttg att ata 257  
 Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile Ser Leu Phe Leu Ile Ile  
 40 45 50  
 35 tcc atg tgt ctt ctc ttc cta tgg aaa aaa tat caa ccc tac aaa gtt 305

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Ser Met Cys Leu Leu Phe Leu Trp Lys Lys Tyr Gln Pro Tyr Lys Val  
 55 60 65 70  
 ata aaa cag aaa cta gaa ggc agg cca gaa aca gaa tac agg aaa got 353  
 ile Lys Gln Lys Leu Glu Gly Arg Pro Glu Thr Glu Tyr Arg Lys Ala  
 5 75 80 85  
 caa aca ttt tca ggc cat gaa gat gct ctg gat gac ttc gga ata tat 401  
 Gln Thr Phe Ser Gly His Glu Asp Ala Leu Asp Asp Phe Gly Ile Tyr  
 90 95 100  
 gaa ttt gtt gct ttt cca gat gtt tct ggt gtt tcc agg atc cca agc 449  
 10 Glu Phe Val Ala Phe Pro Asp Val Ser Gly Val Ser Arg Ile Pro Ser  
 105 110 115  
 agg tct gtt cca gcc tct gat tgt gta tct ggg caa gat ttg cac agt 497  
 Arg Ser Val Pro Ala Ser Asp Cys Val Ser Gly Gln Asp Leu His Ser  
 120 125 130  
 15 aca gtg tat gaa gtt att cag cac atc cct gcc cag cag caa gac cat 545  
 Thr Val Tyr Glu Val Ile Gln His Ile Pro Ala Gln Gln Gln Asp His  
 135 140 145 150  
 cca gag tgaactttca tgggctaaac agtacattcg agtgaatttc tgaagaac 600  
 Pro Glu  
 20  
 attttaagga aaaacagtgg aaaagtatat taatctggaa tcagtgaaga aaccaagacc 660  
 aacacctctt actcattatt cctttacatg cagaatagag gcatttatgc aaattgaact 720  
 gcagggtttt cagcatatac acaatgtctt gtgcaacaga aaacatggtt ggggaaatat 780  
 tcttcagtgg agagtcgttc tcatgctgac ggggagaacg aaagtgcag gggtttcttc 840  
 25 ataagttttg tatgaatat ctctacaaac ctcaattagt tctactctac actttcaact 900  
 tcatcaaacac tgagactatc ctgtctcacc tacaattgtg gaaactttac attgttcgat 960  
 ttttcagcag actttgtttt attaaatttt tattagtgtt aagaatgcta aagtttcaat 1020  
 tttatttcca aattctatc ttgttatttg tacaacaaag taataaggat ggttgcaca 1080  
 aaaacaaaac tatgccttct ctttttttcc aatcaccagt agtatttttg agaagacttg 1140  
 30 tgaacactta aggaatgac tattaaagtc ttatttttat ttttttcaag gaaagatgga 1200  
 ttcaataaaa ttattctgtt ttgttttt 1229  
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 35 <212> PRT

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&lt;213&gt; Homo sapiens

&lt;400&gt; 91

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Ile Gly Ala Val Ile Ala Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val
      20          25          30
Pro Arg Ser Ala Ser Ile Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu
      35          40          45
10  Ala Leu Gln Leu His Pro Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln
      50          55          60
Glu Lys Phe Gln Asp Leu Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser
      65          70          75          80
Glu Lys Arg Lys Gln Tyr Asp Thr Tyr Gly Glu Glu Gly Leu Lys Asp
15      85          90          95
Gly His Gln Ser Ser His Gly Asp Ile Phe Ser His Phe Phe Gly Asp
      100          105          110
Phe Gly Phe Met Phe Gly Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile
      115          120          125
20  Pro Arg Gly Ser Asp Ile Ile Val Asp Leu Glu Val Thr Leu Glu Glu
      130          135          140
Val Tyr Ala Gly Asn Phe Val Glu Val Val Arg Asn Lys Pro Val Ala
      145          150          155          160
Arg Gln Ala Pro Gly Lys Arg Lys Cys Asn Cys Arg Gln Glu Met Arg
25      165          170          175
Thr Thr Gln Leu Gly Pro Gly Arg Phe Gln Met Thr Gln Glu Val Val
      180          185          190
Cys Asp Glu Cys Pro Asn Val Lys Leu Val Asn Glu Glu Arg Thr Leu
      195          200          205
30  Glu Val Glu Ile Glu Pro Gly Val Arg Asp Gly Met Glu Tyr Pro Phe
      210          215          220
Ile Gly Glu Gly Glu Pro His Val Asp Gly Glu Pro Gly Asp Leu Arg
      225          230          235          240
Phe Arg Ile Lys Val Val Lys His Pro Ile Phe Glu Arg Arg Gly Asp
35      245          250          255

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Asp Leu Tyr Thr Asn Val Thr Ile Ser Leu Val Glu Ser Leu Val Gly  
 260 265 270  
 Phe Glu Met Asp Ile Thr His Leu Asp Gly His Lys Val His Ile Ser  
 275 280 285  
 5 Arg Asp Lys Ile Thr Arg Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu  
 290 295 300  
 Gly Leu Pro Asn Phe Asp Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile  
 305 310 315 320  
 Thr Phe Asp Val Asp Phe Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg  
 10 325 330 335  
 Glu Gly Ile Lys Gln Leu Leu Lys Gln Gly Ser Val Gln Lys Val Tyr  
 340 345 350  
 Asn Gly Leu Gln Gly Tyr  
 355  
 15  
 <210> 92  
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 <212> PRT  
 <213> Homo sapience  
 20  
 <400> 92  
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 1 5 10 15  
 Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr  
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 Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala  
 35 40 45  
 Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe  
 50 55 60  
 30 Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile Ala Ile Ser Leu  
 65 70 75 80  
 Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly Ala Tyr Lys Gln  
 85 90 95  
 Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln Ile Phe Asp Phe  
 25 100 105 110

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Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile Tyr Pro Asn Ser  
 115 120 125  
 Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe Pro Tyr Arg Asp  
 130 135 140  
 5 Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu Ile Ile Leu Leu  
 145 150 155 160  
 Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu Ile Ser Cys Val  
 165 170 175  
 Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser Ser Asp Val Leu  
 10 180 185 190  
 Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu Pro Pro Tyr Asp  
 195 200 205  
 Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro Pro Tyr Val  
 210 215 220  
 15 Ser Ala  
 225  
  
 <210> 93  
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 20 <212> PRT  
 <213> Homo sapiens  
  
 <400> 93  
 Met Arg Leu Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg  
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 Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys  
 20 25 30  
 Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser  
 35 40 45  
 30 Xaa Gly Tyr Arg Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln  
 50 55 60  
 Arg Tyr Pro Asp Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro  
 65 70 75 80  
 Ile Tyr Arg His Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu  
 35 85 90 95

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Ile Gly Leu Ile Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met  
                   100                  105                  110  
 Gln Ala Pro Ser Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala  
                   115                  120                  125  
 5 Cys Met Met Val Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met  
                   130                  135                  140  
 Ser Thr Gly Ala Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser  
                   145                  150                  155                  160  
 Lys Leu Glu Ser Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile  
 10                   165                  170                  175  
 Leu Asp Asn Glu Met Lys Leu Asn Val His Met Asp Ser Ile Pro His  
                   180                  185                  190  
 His Arg Ser  
                   195  
 15  
 <210> 94  
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 <212> PRT  
 <213> Homo sapiance  
 20  
 <400> 94  
 Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu  
                   1                  5                  10                  15  
 Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu  
 25                   20                  25                  30  
 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu  
                   35                  40                  45  
 Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu  
                   50                  55                  60  
 30 Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser  
                   65                  70                  75                  80  
 Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu  
                   85                  90                  95  
 Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu  
 35                   100                  105                  110

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Thr Asp Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu  
 115 120 125  
 Phe Gly Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg  
 130 135 140  
 5 Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu  
 145 150 155 160  
 Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His  
 165 170 175  
 Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu  
 10 180 185 190  
 Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His  
 195 200 205  
 Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr  
 210 215 220  
 15 Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn  
 225 230 235 240  
 Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn  
 245 250 255  
 Asn Gly Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu  
 20 260 265 270  
 Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu  
 275 280 285  
 Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp  
 290 295 300  
 25 Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe  
 305 310 315 320  
 Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr  
 325 330 335  
 Lys His Asp  
 30  
 <210> 95  
 <211> 487  
 <212> PRT  
 <213> Homo sapiens  
 35



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&lt;400&gt; 95

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Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys
  1           5           10          15
Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro
5           20           25           30
Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val
  35           40           45
Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser
  50           55           60
10 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu
  65           70           75           80
Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe
  85           90           95
Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu
15           100          105          110
Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala
  115          120          125
Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser
  130          135          140
20 Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu
  145          150          155          160
Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val
  165          170          175
Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala
25           180          185          190
Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile
  195          200          205
Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile
  210          215          220
30 Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val
  225          230          235          240
Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu
  245          250          255
Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala
35           260          265          270

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Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro  
 275 280 285  
 Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser  
 290 295 300  
 5 Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro  
 305 310 315 320  
 Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg  
 325 330 335  
 Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu  
 10 340 345 350  
 Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser  
 355 360 365  
 Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Val Val Pro  
 370 375 380  
 15 Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser  
 385 390 395 400  
 Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu  
 405 410 415  
 Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu  
 20 420 425 430  
 Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu  
 435 440 445  
 Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe  
 450 455 460  
 25 Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser  
 465 470 475 480  
 Glu Leu Ala Ser Gly Pro Pro  
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 30 <210> 96  
 <211> 393  
 <212> PRT  
 <213> Homo sapiens  
 35 <400> 96

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Met Arg Thr Leu Phe Asn Leu Leu Trp Leu Ala Leu Ala Cys Ser Pro  
 1 5 10 15  
 Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala Ala Ser Lys  
 20 25 30  
 5 Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp Lys Pro Val Gln Asp Arg  
 35 40 45  
 Gly Leu Val Val Thr Asp Leu Lys Ala Glu Ser Val Val Leu Glu His  
 50 55 60  
 Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp Arg His Phe Ala Gly Asp  
 10 65 70 75 80  
 Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr Asp Val Thr  
 85 90 95  
 Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val Trp Leu Gln  
 100 105 110  
 15 Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Val Thr Gly Leu His Asp  
 115 120 125  
 Val Asp Gln Gly Trp Met Arg Ala Val Arg Lys His Ala Lys Gly Leu  
 130 135 140  
 His Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr Asp Asp Phe  
 20 145 150 155 160  
 Arg Asn Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu Ser Lys Thr  
 165 170 175  
 Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe Val Val Glu  
 180 185 190  
 25 Val Trp Asn Gln Leu Leu Ser Gln Lys Arg Val Gly Leu Ile His Met  
 195 200 205  
 Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu Leu Ala Leu  
 210 215 220  
 Leu Val Ile Pro Pro Ala Ile Thr Pro Gly Thr Asp Gln Leu Gly Met  
 30 225 230 235 240  
 Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Val Leu Asp Gly Phe  
 245 250 255  
 Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala His Gln Pro Gly Pro Asn  
 260 265 270  
 35 Ala Pro Leu Ser Trp Val Arg Ala Cys Val Gln Val Leu Asp Pro Lys

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275                      280                      285  
 Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe Tyr Gly Met  
 290                      295                      300  
 Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu Pro Val Val Gly Ala Arg  
 5    305                      310                      315                      320  
 Tyr Ile Gln Thr Leu Lys Asp His Arg Pro Arg Met Val Trp Asp Ser  
 325                      330                      335  
 Gln Ala Ser Glu His Phe Phe Glu Tyr Lys Lys Ser Arg Ser Gly Arg  
 340                      345                      350  
 10    His Val Val Phe Tyr Pro Thr Leu Lys Ser Leu Gln Val Arg Leu Glu  
 355                      360                      365  
 Leu Ala Arg Glu Leu Gly Val Gly Val Ser Ile Trp Glu Leu Gly Gln  
 370                      375                      380  
 Gly Leu Asp Tyr Phe Tyr Asp Leu Leu  
 15    385                      390  
  
 <210> 97  
 <211> 196  
 <212> PRT  
 20    <213> Homo sapience  
  
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 25    Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr Leu Ala  
 20                      25                      30  
 Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro Gly Gly  
 35                      40                      45  
 Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile Thr Gly  
 30    50                      55                      60  
 Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln Val Lys  
 65                      70                      75                      80  
 Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly Asn Thr  
 85                      90                      95  
 35    Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val Phe Val

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100 105 110  
 Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser Lys Asp  
 115 120 125  
 Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser Ala Tyr  
 5 130 135 140  
 Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln Tyr Gln  
 145 150 155 160  
 Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro Leu Glu  
 165 170 175  
 10 Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala Asn Ser  
 180 185 190  
 Pro Val Gly Arg  
 195  
 15 <210> 98  
 <211> 107  
 <212> PRT  
 <213> Homo sapience  
 20 <400> 98  
 Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met Ser  
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 Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly Ser  
 20 25 30  
 25 Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly Ile  
 35 40 45  
 Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys Ser  
 50 55 60  
 Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val Ala  
 30 65 70 75 80  
 Ala Glu Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr Ser  
 85 90 95  
 Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro  
 100 105  
 35

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<210> 99  
 <211> 350  
 <212> PRT  
 <213> Homo sapiens

5

&lt;400&gt; 99

Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly Pro Lys Gly Ala Pro  
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 Ala Ala Glu Pro Gly Lys Arg Ser Glu Gly Gly Lys Thr Pro Val Ala  
 10 20 25 30  
 Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro Arg Thr Cys Leu Ser  
 35 40 45  
 Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala Trp Phe Val Phe Gln  
 50 55 60  
 15 Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln Tyr Gln Leu Leu Lys  
 65 70 75 80  
 Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser Lys Ile Ser Leu Ile  
 85 90 95  
 Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met Glu Gln Leu Lys Ser  
 20 100 105 110  
 Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln Glu Glu Ile Asn Glu  
 115 120 125  
 Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys Gln Asp Ile Leu Asn  
 130 135 140  
 25 Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr Lys Val Asp Gln Ser  
 145 150 155 160  
 Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys Ile Thr Ser Val Lys  
 165 170 175  
 Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr Asp Val Ile Ser Leu  
 30 180 185 190  
 Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile Glu Lys Val Glu Lys  
 195 200 205  
 Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser Ser Ser Ile Asp Arg  
 210 215 220  
 35 Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn Ser Gln Arg Ile Asn

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225                      230                      235                      240  
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 5                      260                      265                      270  
 Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys Val Tyr Asn Leu Lys  
                          275                      280                      285  
 Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn Asp Leu Thr Leu Arg  
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 10    Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg Glu Lys Glu Ile Ala  
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 Ile Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu  
                          35                      40                      45  
 Ser Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val  
 30                      50                      55                      60  
 Asn Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu  
                          65                      70                      75                      80  
 Leu Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly  
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 35    Arg Pro Ala Gly Gly Ala His Leu Cys Ala Ala

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100

105

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 ctcatgatcc tgatatgtgc tatggctact taaggagcgt acaagcaacg cgcagcctgg 300  
 atcatcccat tcttctgtta ccagatcttt gactttgccc tgaacatgtt ggttgcaatc 360  
 5 actgtgctta tttatccaaa ctccattcag gaatacatac ggcaactgcc tccaaatttt 420  
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&lt;210&gt; 103

&lt;211&gt; 585

&lt;212&gt; DNA

15 &lt;213&gt; Homo Sapiens

&lt;400&gt; 103

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 25 aaccagtgtg tgcacacagg tgcatttgag ataacttta atgatgtacc tgtgtggtct 480  
 aagctggaat ctggtagcct tccatccatg caacaacttg tcaaatctt tgacaatgaa 540  
 atgaagctca atgtgcatat ggattcaatc ccacaccatc gatca 585

&lt;210&gt; 104

30 &lt;211&gt; 1017

&lt;212&gt; DNA

&lt;213&gt; Homo Sapiens

&lt;400&gt; 104

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	ggacgacgcc cagaatggga gctgactgat atggtggtgt gggtagctgg agcctcgagt	180
	ggaattggtg aggagctggc ttaccagttg tctaaactag gagtctctct tgtgctgtca	240
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	tcccacaaga tgacaaccag tcgttgtgtg cggtgatgt taatcagcat ggccaatgat	840
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	agggccctcg agagccaaag cgtgaccccc aagccactgg agactgagcc tagcagggag	180
	accgcctggt ccataggcct tcaggtgacc gtgcccttca tgtttgcagg cctgggactg	240
	tcctgggccc geatgottct ggaactattc cagcaactggc ctgtgtttgt ggaggtgaaa	300
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	gtggagtgtc tgtgtgccag cagtgtctc actgccttcc ttgcagcctt tgcctggggg	600
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	cacttcttcg agtacaagaa gagccgcagt gggaggcacg tcgtcttcta cccaacctg	1080
	aagtccctgc aggtgcggtt ggagctggcc cgggagctgg gcgttggggc ctctatctgg	1140
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	gaggagtgtg tggaacagga cccgggacag aggaacc atg got cag aac otg	175
	Met Ala Pro Gln Asn Leu	
	1 5	
	agc acc ttt tgc ctg ttg ctg cta tac ctc atc ggg gcg gtg att gcc	223
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	Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val Pro Arg Ser Ala Ser Ile	
	25 30 35	
25	aag gat att aaa aag gcc tat agg aaa cta gcc ctg cag ctt cat ccc	319
	Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu Ala Leu Gln Leu His Pro	
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	Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln Glu Lys Phe Gln Asp Leu	
30	55 60 65 70	
	ggt gct gct tat gag gtt ctg tca gat agt gag aaa cgg aaa cag tac	415
	Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser Glu Lys Arg Lys Gln Tyr	
	75 80 85	
	gat act tat ggt gaa gaa gga tta aaa gat ggt cat cag agc tcc cat	463
35	Asp Thr Tyr Gly Glu Glu Gly Leu Lys Asp Gly His Gln Ser Ser His	

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	gga gac att ttt tca cac ttc ttt ggg gat ttt ggt ttc atg ttt gga			511
	Gly Asp Ile Phe Ser His Phe Phe Gly Asp Phe Gly Phe Met Phe Gly			
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5	gga acc cct cgt cag caa gac aga aat att cca aga gga agt gat att			559
	Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile Pro Arg Gly Ser Asp Ile			
	120	125	130	
	att gta gat cta gaa gtc act ttg gaa gaa gta tat gca gga aat ttt			607
	Ile Val Asp Leu Glu Val Thr Leu Glu Glu Val Tyr Ala Gly Asn Phe			
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	gtg gaa gta gtt aga aac aaa cct gtg gca agg cag gct cct ggc aaa			655
	Val Glu Val Val Arg Asn Lys Pro Val Ala Arg Gln Ala Pro Gly Lys			
	155	160	165	
	egg aag tgc aat tgt cgg caa gag atg cgg acc acc cag ctg ggc cct			703
15	Arg Lys Cys Asn Cys Arg Gln Glu Met Arg Thr Thr Gln Leu Gly Pro			
	170	175	180	
	ggg cgc ttc caa atg acc cag gag gtg gtc tgc gac gaa tgc cct aat			751
	Gly Arg Phe Gln Met Thr Gln Glu Val Val Cys Asp Glu Cys Pro Asn			
	185	190	195	
20	gtc aaa cta gtg aat gaa gaa cga acg ctg gaa gta gaa ata gag cct			799
	Val Lys Leu Val Asn Glu Glu Arg Thr Leu Glu Val Glu Ile Glu Pro			
	200	205	210	
	ggg gtg aga gac ggc atg gag tac ccc ttt att gga gaa ggt gag cct			847
	Gly Val Arg Asp Gly Met Glu Tyr Pro Phe Ile Gly Glu Gly Glu Pro			
25	215	220	225	230
	cac gtg gat ggg gag cct gga gat tta cgg ttc cga atc aaa gtt gtc			895
	His Val Asp Gly Glu Pro Gly Asp Leu Arg Phe Arg Ile Lys Val Val			
	235	240	245	
	aag cac cca ata ttt gaa agg aga gga gat gat ttg tac aca aat gtg			943
30	Lys His Pro Ile Phe Glu Arg Arg Gly Asp Asp Leu Tyr Thr Asn Val			
	250	255	260	
	aca atc tca tta gtt gag tca ctg gtt ggc ttt gag atg gat att act			991
	Thr Ile Ser Leu Val Glu Ser Leu Val Gly Phe Glu Met Asp Ile Thr			
	265	270	275	
35	cac ttg gat ggt cac aag gta cat att tcc cgg gat aag atc acc agg			1039

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	Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu Gly Leu Pro Asn Phe Asp	
5	295 300 305 310	
	aac aac aat atc aag ggc tct ttg ata atc act ttt gat gtg gat ttt	1135
	Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile Thr Phe Asp Val Asp Phe	
	315 320 325	
	cca aaa gaa cag tta aca gag gaa gcg aga gaa ggt atc aaa cag cta	1183
10	Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg Glu Gly Ile Lys Gln Leu	
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	ctg aaa caa ggg tca gtg cag aag gta tac aat gga ctg caa gga tat	1231
	Leu Lys Gln Gly Ser Val Gln Lys Val Tyr Asn Gly Leu Gln Gly Tyr	
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	ttttatctaa tgatcatcat gaaatgaata agagggttta agaatttgct catttgcatt	1410
	cggaaaagaa tgaccagcaa aagggtttact aatacctctc cctttgggga tttaatgtct	1470
	ggtgtgtccg cctgagtttc aagaattaaa gctgcaagag gactccagga gcaaaagaaa	1530
20	cacaatatag agggttggag ttgttagcaa ttccattcaa aatgcccaact ggagaagtct	1590
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	agcgaagggt accgaccctgg cagaagctcg gactctcggg ggtatcgagg aggcaggccc	120
	gggggcgcac gggcgagcgg gccgggagcc ggagcggcgg aggagccggc agcagcggcg	180
35	cggcgggctc caggcgaggg ggtcgacgct cctgaaaaact tcgcgcgcgg ctcgcgccac	240



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	tgccgccgga gcg atg aag atg gtc gcg ccc tgg acg cgg ttc tac tcc	289
	Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser	
	1 5 10	
	aac agc tgc tgc ttg tgc tgc cat gtc cgc acc ggc acc atc ctg etc	337
5	Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu	
	15 20 25	
	ggc gtc tgg tat ctg atc atc aat gct gtg gta ctg ttg att tta ttg	385
	Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu	
	30 35 40	
10	agt gcc ctg gct gat ccg gat cag tat aac ttt tca agt tct gaa ctg	433
	Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu	
	45 50 55 60	
	gga ggt gac ttt gag ttc atg gat gat gcc aac atg tgc att gcc att	481
	Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile	
15	65 70 75	
	gcg att tct ctt etc atg atc ctg ata tgt gct atg gct act tac gga	529
	Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly	
	80 85 90	
	gcg tac aag caa cgc gca gcc tgg atc atc cca ttc ttc tgt tac cag	577
20	Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln	
	95 100 105	
	atc ttt gac ttt gcc ctg aac atg ttg gtt gca atc act gtg ctt att	625
	Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile	
	110 115 120	
25	tat cca aac tcc att cag gaa tac ata cgg caa ctg cct cct aat ttt	673
	Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe	
	125 130 135 140	
	ccc tac aga gat gat gtc atg tca gtg aat cct acc tgt ttg gtc ott	721
	Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu	
30	145 150 155	
	att att ctt ctg ttt att agc att atc ttg act ttt aag ggt tac ttg	769
	Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu	
	160 165 170	
	att agc tgt gtt tgg aac tgc tac cga tac atc aat ggt agg aac tcc	817
35	Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser	

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	175	180	185	
	tot gat gtc ctg gtt tat gtt acc agc aat gac act acg gtg ctg cta	865		
	Ser Asp Val Leu Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu			
	190	195	200	
5	ccc ccg tat gat gat gcc act gtg aat ggt gct gcc aag gag cca ccg	913		
	Pro Pro Tyr Asp Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro			
	205	210	215	220
	cca cct tac gtg tct gcc taagccttca agtgggcgga gctgagggc	960		
	Pro Pro Tyr Val Ser Ala			
10	225			
	agcagcttga ctttgcagac atctgagcaa tagttctgtt atttcaacttt tgccatgagc	1020		
	ctctctgagc ttgtttgttg ctgaaatgct acctttttaa atttagatgt tagattgaaa	1080		
	actgtatgtt tcaacatatc ctttgcctgga acactgtgat agattaactg tagaattctt	1140		
	cctgtacgat tggggatata atgggcttca ctaaccttcc ctaggcattg aaacttcccc	1200		
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	ttctctctgt tccctctctt ttgaaaatgt aaaataaaac caaaaataga caacttttcc	1320		
	ttcagccatt ccagcataga gaacaaaacc ttatggaaac aggaatgtca attgtgtaat	1380		
	cattgttcta attaggtaaa tagaagtctt tatgtatgtg ttacaagaat ttccccca	1440		
	acatccttta tgactgaagt tcaatgacag tttgtgtttg gtggtaaagg attttctcca	1500		
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	tgttcttgtg gatcttgtgt ccagggacat ggggtgacat gcctcgtatg tgttagagg	1620		
	tggaatggat gtgtttggcg ctgcatggga tctggtgccc ctcttctcct ggattcacat	1680		
	ccccacccag ggcctgcttt tactaagtgt tctgcctag attggttcaa ggaggtcatc	1740		
	caactgactt tatcaagtgg aattgggata tatttgatat acctctgoot aacaacatgg	1800		
25	aaaagggttt tcttttccct gcaagctaca tctactgct ttgaacttcc aagtatgtct	1860		
	agtcaccttt taaaatgtaa acattttcag aaaaatgagg attgccttcc ttgtatggc	1920		
	tttttacctt gactacctga attgcaaggg atttttatat attcatatgt tacaagaatca	1980		
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	<213> Homo Sapiens			
35	<220>			

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&lt;221&gt; CDS

&lt;222&gt; (43)...(630)

&lt;400&gt; 113

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                                     Met Arg Leu Leu
                                     1
ctg ctt ctc cta gtg gcg gcg tct gcg atg gtc cgg agc gag gcc tcg      102
Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Glu Ala Ser
10  5          10          15          20
gcc aat ctg ggc ggc gtg ccc agc aag aga tta aag atg cag tac gcc      150
Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala
          25          30          35
acg ggg ccg ctg ctc aag ttc cag att tgt gtt tcc tga ggt tat agg      198
15  Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser Xaa Gly Tyr Arg
          40          45          50
cgg gtg ttt gag gag tac atg cgg gtt att agc cag cgg tac cca gac      246
Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln Arg Tyr Pro Asp
          55          60          65
20  atc cgc att gaa gga gag aat tac ctc cct caa cca ata tat aga cac      294
Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro Ile Tyr Arg His
          70          75          80
ata gca tot ttc ctg tca gtc ttc aaa cta gta tta ata ggc tta ata      342
Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu Ile Gly Leu Ile
25  85          90          95          100
att gtt ggc aag gat cct ttt gct ttc ttt ggc atg caa gct cct agc      390
Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met Gln Ala Pro Ser
          105          110          115
30  atc tgg cag tgg ggc caa gaa aat aag gtt tat gca tgt atg atg gtt      438
Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala Cys Met Met Val
          120          125          130
tto ttc ttg agc aac atg att gag aac cag tgt atg tca aca ggt gca      486
Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met Ser Thr Gly Ala
          135          140          145
35  ttt gag ata act tta aat gat gta cct gtg tgg tot aag ctg gaa tct      534

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Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser Lys Leu Glu Ser

5	165	170	175	180
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Met Lys Leu Asn Val His Met Asp Ser Ile Pro His His Arg Ser

**185**

10 agcagcgtga ctgacattat gaaggcctgt actgaagaca gcaagctgtt agtacagacc 740

cagtgcctggc atattttgga attctgcaca ttcattggagt gcaataatac tgtatagctt 860

acattactac ttgtacttt ttttcttagt catatttgaa aaagtagaaa attgagttac 980

15 aatttgattt ttttccaaa gatgtctgtt aaatctgttg tgcttttata tgaatatttg 1040

ttttttatag tttaaaattg atcctttggg aatccagttg aagttcccaa atactttata 1100

agagttttatc agacatctct aatttggcca tgtccagttt ataccagttta caaaatatag 1160

cagatgcaag attatgqqqq aaatcctata ttcagagtac tctataaatt tttgtgtatg 1220

tgtgtatgtg cgtgtgatta ccagagaact actaaaaaaa ccaactgctt tttaaatcct 1280

20 attgtgtagt taaagtgtca tgccttgacc aatctaataa attgattaat taactgggcc 1340

tttatactta actaaataaa aaactaaqca gatatgagtt 1380

**<210> 114**

&lt;211&gt; 1292

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<213> Homo Sapience

**<220>**

**<221> CDS**

**<222> (113)...(1132)**

30

**<400> 114**

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gactctggtg cgggcgtct tcttcccc gagctgggcg tgcgcggccg ca atg aac 118

Met Asn

35

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	tgg gag ctg ctg ctg tgg ctg ctg gtg ctg tgc gcg ctg etc etc	166
	Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu Leu	
	5 10 15	
5	ttg gtg cag ctg ctg cgc ttc ctg agg gct gac ggc gac ctg acg cta	214
	Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu	
	20 25 30	
	cta tgg gcc gag tgg cag gga cga cgc cca gaa tgg gag ctg act gat	262
	Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp	
	35 40 45 50	
10	atg gtg gtg tgg gtg act gga gcc tcg agt gga att ggt gag gag ctg	310
	Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu	
	55 60 65	
	gct tac cag ttg tct aaa cta gga gtt tct ctt gtg ctg tca gcc aga	358
	Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg	
15	70 75 80	
	aga gtg cat gag ctg gaa agg gtg aaa aga aga tgc cta gag aat ggc	406
	Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly	
	85 90 95	
	aat tta aaa gaa aaa gat ata ctt gtt ttg ccc ctt gac ctg acc gac	454
20	Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp	
	100 105 110	
	act ggt tcc cat gaa gcg gct acc aaa gct gtt ctc cag gag ttt ggt	502
	Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu Phe Gly	
	115 120 125 130	
25	aga atc gac att ctg gtc aac aat ggt gga atg tcc cag cgt tct ctg	550
	Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg Ser Leu	
	135 140 145	
	tgo atg gat acc agc ttg gat gtc tac aga aag cta ata gag ctt aac	598
	Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu Leu Asn	
30	150 155 160	
	tac tta ggg acg gtg tcc ttg aca aaa tgt gtt ctg cct cac atg atc	646
	Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile	
	165 170 175	
	gag agg aag caa gga aag att gtt act gtg aat agc atc ctg ggt atc	694
35	Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile	

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	180	185	190	
	ata tct gta cct ctt tcc att gga tac tgt gct agc aag cat gct ctc	742		
	Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu			
	195	200	205	210
5	cgg ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cca ggt	790		
	Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly			
	215	220	225	
	ata ata gtt tct aac att tgc cca gga cct gtg caa tca aat att gtg	838		
	Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn Ile Val			
10	230	235	240	
	gag aat tcc cta gct gga gaa gtc aca aag agt ata ggc aat aat gga	886		
	Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly			
	245	250	255	
	gac cag tcc cac aag atg aca acc agt cgt tgt gtg cgg ctg atg tta	934		
15	Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu			
	260	265	270	
	atc agc atg gcc aat gat ttg aaa gaa gtt tgg atc tca gaa caa cct	982		
	Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro			
	275	280	285	290
20	ttc ttg tta gta aca tat ttg tgg caa tac atg cca acc tgg gcc tgg	1030		
	Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp Ala Trp			
	295	300	305	
	tgg ata acc aac aag atg ggg aag aaa agg att gag aac ttt aag agt	1078		
	Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser			
25	310	315	320	
	ggt gtg gat gca gac tct tct tat ttt aaa atc ttt aag aca aaa cat	1126		
	Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr Lys His			
	325	330	335	
30	gac tgaanagac atctgtactt ttcaagccac tggagggaaa aatggaaaac a	1180		
	Asp			
	tgaaaacagc aatcttctta tgcttctgaa taatcaaga ctaatttggt gttttacttt	1240		
	ttaatagata tgactttgct tccaacatgy aatgaataaa aaaataagta at	1292		
35	<210> 115			

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 Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys  
 1 5 10 15  
 cca ggg gag ctg ggg ctt cct cac ccc ctc agc aca gga gga ctc cct 151  
 Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro  
 15 20 25 30  
 gta gcc tca gaa gat gga gct ctc agg gcc cct gag agc caa agc gtg 199  
 Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val  
 35 40 45  
 acc ccc aag cca ctg gag act gag cct agc agg gag acc gcc tgg tcc 247  
 20 Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser  
 50 55 60  
 ata ggc ctt cag gtg acc gtg ccc ttc atg ttt gca ggc ctg gga ctg 295  
 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu  
 65 70 75 80  
 25 tcc tgg gcc ggc atg ctt ctg gac tat ttc cag cac tgg cct gtg ttt 343  
 Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe  
 85 90 95  
 gtg gag gtg aaa gac ctt ttg aca ttg gtg ccg ccc ctg gtg ggc ctg 391  
 Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu  
 30 100 105 110  
 aag ggg aac ctg gag atg aca ctg gca tcc aga ctc tcc aca gct gcc 439  
 Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala  
 115 120 125  
 aac act gga caa att gat gac ccc cag gag cag cac aga gtc atc agc 487  
 35 Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser

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	130	135	140	
	agc aac ctg gcc ctc atc cag gtg cag gcc act gtc gtg ggg ctc ttg	535		
	Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu			
	145	150	155	160
5	gct gct gtg gct gcg ctg ctg ttg ggc gtg gtg tct cga gag gaa gtg	583		
	Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val			
	165	170	175	
	gat gtc gcc aag gtg gag ttg ctg tgt gcc agc agt gtc ctc act gcc	631		
	Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala			
10	180	185	190	
	ttc ctt gca gcc ttt gcc ctg ggg gtg ctg atg gtc tgt ata gtg att	679		
	Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile			
	195	200	205	
	ggc gct cga aag ctc ggg gtc aac cca gac aac att gcc acg ccc att	727		
15	Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile			
	210	215	220	
	gca gcc agc ctg gga gac ctc atc aca ctg tcc att ctg gct ttg gtt	775		
	Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val			
	225	230	235	240
20	agc agc ttc ttc tac aga cac aaa gat agt cgg tat ctg acg ccg ctg	823		
	Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu			
	245	250	255	
	gtc tgc ctc agc ttt gcg gct ctg acc cca gtg tgg gtc ctc att gcc	871		
	Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala			
25	260	265	270	
	aag cag agc cca ccc atc gtg aag atc ctg aag ttt ggc tgg ttc cca	919		
	Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro			
	275	280	285	
	atc atc ctg gcc atg gtc atc agc agt ttc gga gga ctc atc ttg agc	967		
30	Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser			
	290	295	300	
	aaa acc gtt tct aaa cag cag tac aaa ggc atg gcg ata ttt acc ccc	1015		
	Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro			
	305	310	315	320
35	gtc ata tgt ggt gtt cgt gcc aat ctg gtg gcc att cag acc agc cga	1063		



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	325 330 335	
	atc tca acc tac ctg cac atg tgg agt gca cct ggc gtc ctg ccc etc	1111
	Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu	
5	340 345 350	
	cag atg aag aaa ttc tgg ccc aac ccg tgt tct act ttc tgc acg tca	1159
	Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser	
	355 360 365	
	gaa atc aat tcc atg tca gct cga gtc ctg etc ttg ctg gtg gtc cca	1207
10	Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Leu Val Val Pro	
	370 375 380	
	ggc cat ctg att ttc ttc tac atc atc tac ctg gtg gag ggt cag tca	1255
	Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser	
	385 390 395 400	
15	gtc ata aac agc cag acc ttt gtg gtg etc tac ctg ctg gca ggc ctg	1303
	Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu	
	405 410 415	
	atc cag gtg aca atc ctg ctg tac ctg gca gaa gtg atg gtt cgg ctg	1351
	Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu	
20	420 425 430	
	act tgg cac cag gcc ctg gat cct gac aac cac tgc atc ccc tac ctt	1399
	Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu	
	435 440 445	
	aca ggg ctg ggg gac ctg etc ggt act ggc etc ctg gca etc tgc ttt	1447
25	Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe	
	450 455 460	
	ttc act gac tgg cta ctg aag agc aag gca gag ctg ggt ggc atc tca	1495
	Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser	
	465 470 475 480	
30	gaa ctg gca tct gga cct ccc taactgggccc ccgctgggtcc catttgetca ttag	1550
	Glu Leu Ala Ser Gly Pro Pro	
	485	
	aatttcctct caccatcagtg ggatacagaa ttcagtttct cccttgccag gtccttggga	1610
	tggttgaccc ctgcctctgc agtagccttt tgtgagctcg ctaaggtagc tctcacacac	1670
35	ctcggtctcg gggttgatac ctgagcctgc aatagagccc tgaatcaag agcatggctt	1730

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 ggggtgtgtt gtctttttcc atgcccctgc aacccagatt ggggtggagg aggaaggagg 1910  
 tctttctgt tcccaagcct cagaactctt gagctgtggc ttacttctgt tcttcaccag 1970  
 5 gtccaagctc cgtggggccac actgtgtgtg tgccaagaag gtgtacagcc tccccaggat 2030  
 ggggcctcat acaacccttc atctgcactc aacatttaac cgtgtccttg ctgtcttttt 2090  
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 taaaacagat tatattgt 2168

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15 <221> CDS  
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 Met Arg Thr Leu Phe Asn Leu Leu Trp Leu  
 1 5 10  
 gcc ctg gcc tgc agc cct gtt cac act acc ctg tca aag tca gat gcc 158  
 Ala Leu Ala Cys Ser Pro Val His Thr Thr Leu Ser Lys Ser Asp Ala  
 25 15 20 25  
 aaa aaa gcc gcc tca aag acg ctg ctg gag aag agt cag ttt tca gat 203  
 Lys Lys Ala Ala Ser Lys Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp  
 30 30 35 40  
 aag ccg gtg caa gac cgg ggt ttg gtg gtg acg gac etc aaa gct gag 254  
 Lys Pro Val Gln Asp Arg Gly Leu Val Val Thr Asp Leu Lys Ala Glu  
 45 50 55  
 agt gtg gtt ctt gag cat cgc agc tac tgc tgg gca aag gcc cgg gac 302  
 Ser Val Val Leu Glu His Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp  
 60 65 70  
 35 aga cac ttt gct ggg gat gta ctg ggc tat gtc act cca tgg aac agc 350

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	Arg	His	Phe	Ala	Gly	Asp	Val	Leu	Gly	Tyr	Val	Thr	Pro	Trp	Asn	Ser	
	75						80					85					90
	cat	ggc	tac	gat	gtc	acc	aag	gtc	ttt	ggg	agc	aag	ttc	aca	cag	atc	398
	His	Gly	Tyr	Asp	Val	Thr	Lys	Val	Phe	Gly	Ser	Lys	Phe	Thr	Gln	Ile	
5					95					100					105		
	tca	ccc	gtc	tgg	ctg	cag	ctg	aag	aga	cgt	ggc	cgt	gag	atg	ttt	gag	446
	Ser	Pro	Val	Trp	Leu	Gln	Leu	Lys	Arg	Arg	Gly	Arg	Glu	Met	Phe	Glu	
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	gtc	acg	ggc	ctc	cac	gac	gtg	gac	caa	ggg	tgg	atg	cga	gct	gtc	agg	494
10	Val	Thr	Gly	Leu	His	Asp	Val	Asp	Gln	Gly	Trp	Met	Arg	Ala	Val	Arg	
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	aag	cat	gcc	aag	ggc	ctg	cac	ata	gtg	cct	cgg	ctc	ctg	ttt	gag	gac	542
	Lys	His	Ala	Lys	Gly	Leu	His	Ile	Val	Pro	Arg	Leu	Leu	Phe	Glu	Asp	
					140					145					150		
15	tgg	act	tac	gat	gat	ttc	cgg	aac	gtc	tta	gac	agt	gag	gat	gag	ata	590
	Trp	Thr	Tyr	Asp	Asp	Phe	Arg	Asn	Val	Leu	Asp	Ser	Glu	Asp	Glu	Ile	
					155					160					170		
	gag	gag	ctg	agc	aag	acc	gtg	gtc	cag	gtg	gca	aag	aac	cag	cat	ttc	638
	Glu	Glu	Leu	Ser	Lys	Thr	Val	Val	Gln	Val	Ala	Lys	Asn	Gln	His	Phe	
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	gat	ggc	ttc	gtg	gtg	gag	gtc	tgg	aac	cag	ctg	cta	agc	cag	aag	cgc	686
	Asp	Gly	Phe	Val	Val	Glu	Val	Trp	Asn	Gln	Leu	Leu	Ser	Gln	Lys	Arg	
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	gtg	ggc	ctc	atc	cac	atg	ctc	acc	cac	ttg	gcc	gag	gct	ctg	cac	cag	734
25	Val	Gly	Leu	Ile	His	Met	Leu	Thr	His	Leu	Ala	Glu	Ala	Leu	His	Gln	
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	Ala	Arg	Leu	Leu	Ala	Leu	Leu	Val	Ile	Pro	Pro	Ala	Ile	Thr	Pro	Gly	
					220					225					230		
30	acc	gac	cag	ctg	ggc	atg	ttc	acg	cac	aag	gag	ttt	gag	cag	ctg	gcc	830
	Thr	Asp	Gln	Leu	Gly	Met	Phe	Thr	His	Lys	Glu	Phe	Glu	Gln	Leu	Ala	
					235					240					245		
	ccc	gtg	ctg	gat	ggg	ttc	agc	ctc	atg	acc	tac	gac	tac	tct	aca	gcg	878
	Pro	Val	Leu	Asp	Gly	Phe	Ser	Leu	Met	Thr	Tyr	Asp	Tyr	Ser	Thr	Ala	
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	cat cag cct ggc cct eat gca ccc ctg tcc tgg gtt cga gcc tgc gtc	926
	His Gln Pro Gly Pro Asn Ala Pro Leu Ser Trp Val Arg Ala Cys Val	
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	cag gtc ctg gac cag aag tcc aag tgg cga agc aaa atc ctc ctg ggg	974
5	Gln Val Leu Asp Pro Lys Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly	
	285 290 295	
	ctc aac ttc tat ggt atg gac tac gcg acc tcc aag gat gcc cgt gag	1022
	Leu Asn Phe Tyr Gly Met Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu	
	300 305 310	
10	cct gtt gtc ggg gcc agg tac atc cag aca ctg aag gac cac agg ccc	1070
	Pro Val Val Gly Ala Arg Tyr Ile Gln Thr Leu Lys Asp His Arg Pro	
	315 320 325 330	
	cgg atg gtg tgg gac agc cag gcc tca gag cac ttc ttc gag tac aag	1118
	Arg Met Val Trp Asp Ser Gln Ala Ser Glu His Phe Phe Glu Tyr Lys	
15	335 340 345	
	aag agc cgc agt ggg agg cac gtc gtc ttc tac cca acc ctg aag tcc	1166
	Lys Ser Arg Ser Gly Arg His Val Val Phe Tyr Pro Thr Leu Lys Ser	
	350 355 360	
	ctg cag gtg cgg ctg gag ctg gcc cgg gag ctg ggc gtt ggg gtc tot	1214
20	Leu Gln Val Arg Leu Glu Leu Ala Arg Glu Leu Gly Val Gly Val Ser	
	365 370 375	
	atc tgg gag ctg gcc cag gcc ctg gac tac ttc tac gac ctg ctc t	1260
	Ile Trp Glu Leu Gly Gln Gly Leu Asp Tyr Phe Tyr Asp Leu Leu	
	380 385 390	
25	aggtgggcat tgcggcctcc gcggtggacg tggtcttttc taagccatgg agtgagtgag	1320
	caggtgtgaa atacaggcct ccaactccgtt tgctgtg	1357
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5	gag agc cct ggg atg cac cgg cca gag gcc atg ctg ctg ctg ctc acg 97
	Glu Ser Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr
	15 20 25 30
	ctt gcc ctc ctg ggg ggc ccc acc tgg gca ggg aag atg tat ggc cct 145
	Leu Ala Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro
10	35 40 45
	gga gga ggc aag tat ttc agc acc act gaa gac tac gac cat gaa atc 193
	Gly Gly Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile
	50 55 60
	aca ggg ctg cgg gtg tct gta ggt ctt ctc ctg gtg aaa agt gtc cag 241
15	Thr Gly Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln
	65 70 75
	gtg aaa ctt gga gac tcc tgg gac gtg aaa ctg gga gcc tta ggt ggg 289
	Val Lys Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly
	80 85 90
20	aat acc cag gaa gtc acc ctg cag cca ggc gaa tac atc aca aaa gtc 337
	Asn Thr Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val
	95 100 105 110
	ttt gtc gcc ttc caa gct ttc ctc cgg ggt atg gtc atg tac acc agc 385
	Phe Val Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser
25	115 120 125
	aag gac cgc tat ttc tat ttt ggg aag ctt gat ggc cag atc tcc tct 433
	Lys Asp Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser
	130 135 140
	gcc tac ccc agc caa gag ggg cag gtg ctg gtg ggc atc tat ggc cag 481
30	Ala Tyr Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln
	145 150 155
	tat caa ctc ctt ggc atc aag agc att ggc ttt gaa tgg aat tat cca 529
	Tyr Gln Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro
	160 165 170
35	cta gag gag ccg acc act gag cca cca gtt aat ctc aca tac tca gca 577

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Leu Glu Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala  
 175 180 185 190  
 aac tca ccc gtg ggt cgc taggggtggg tatggggcca tccgagctga ggcca 630  
 Asn Ser Pro Val Gly Arg  
 5 195  
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 g atg gag cag aag ctt gtg gag gag att ctt caa gca atc act atg 286  
 Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met  
 1 5 10 15  
 25 tca aca gac aca ggt gtt tcc ctt cct tca tat gag gaa gat cag gga 334  
 Ser Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly  
 20 25 30  
 tca aaa etc att cga aaa gct aaa gag gca cca ttc gta ccc gtt gga 382  
 Ser Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly  
 30 35 40 45  
 ata gcg ggt ttt gca gca att gtt gca tat gga tta tat aaa ctg aag 430  
 Ile Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys  
 50 55 60  
 agc agg gga aat act aaa atg tcc att cat ctg atc cac atg cgt gtg 478  
 25 Ser Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val

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	65	70	75	
	gca gcc caa ggc ttt gtt gta gga gca atg act gtt ggt atg ggc tat	526		
	Ala Ala Gln Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr			
	80	85	90	95
5	tcc atg tat cgg gaa ttc tgg gca aaa cct aag cct tagaagaa	570		
	Ser Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro			
	100	105		
	gagatgctgt cttggtcttg ttggaggagc ttgctttagt tagatgtctt attattaaag	630		
	ttacctatta ttgt:ggaaa t	651		
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	tcttaggggc tccagac atg tct gag gtg aag agc cgg aag aag tgg ggg	110		
	Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly			
	1	5	10	
	ccc aag gga gcc cct gct gcg gag ccc ggg aag cgg agc gag ggc ggg	158		
25	Pro Lys Gly Ala Pro Ala Ala Glu Pro Gly Lys Arg Ser Glu Gly Gly			
	15	20	25	
	aag acc ccc gtg gcc cgg agc agc gga ggc ggg ggc tgg gca gac ccc	206		
	Lys Thr Pro Val Ala Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro			
	30	35	40	
30	cga acg tgc ctg agc ctg ctg tgg ctg ggg acg tgc ctg ggc ctg gcc	254		
	Arg Thr Cys Leu Ser Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala			
	45	50	55	
	tgg ttt gta ttt cag cag tca gaa aaa ttt gca aag gtg gaa aac caa	302		
	Trp Phe Val Phe Gln Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln			
35	60	65	70	75

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	tac cag tta ctg aaa cta gaa acc aat gaa ttc caa caa ctt caa agt	350
	Tyr Gln Leu Leu Lys Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser	
	80 85 90	
	aaa atc agt tta att tca gaa aag tgg cag aaa tct gaa gct atc atg	398
5	Lys Ile Ser Leu Ile Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met	
	95 100 105	
	gaa caa ttg aag tct ttt caa ata att gct cat cta aag cgt cta cag	446
	Glu Gln Leu Lys Ser Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln	
	110 115 120	
10	gaa gaa att aat gag gta aaa act tgg tcc aat agg ata act gaa aaa	494
	Glu Glu Ile Asn Glu Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys	
	125 130 135	
	cag gat ata ctg aac aac agt ctg acg acg ctt tct caa gac att aca	542
	Gln Asp Ile Leu Asn Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr	
15	140 145 150 155	
	aaa gta gac caa agt aca act tcc atg gca aaa gat gtt ggt ctc aag	590
	Lys Val Asp Gln Ser Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys	
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20	Ile Thr Ser Val Lys Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr	
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	gat gta ata tca ttg aca gat tct gtg caa gaa cta gaa aat aaa ata	686
	Asp Val Ile Ser Leu Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile	
	190 195 200	
25	gag aaa gta gaa aaa aat aca gta aaa aat ata ggt gat ctt ctt tca	734
	Glu Lys Val Glu Lys Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser	
	205 210 215	
	agc agt att gat cga aca gca acg ctc cga aag aca gca tct gaa aat	782
	Ser Ser Ile Asp Arg Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn	
30	220 225 230 235	
	tca caa aga att aac tct gtt aag aag acg cta acc gaa cta aag agt	830
	Ser Gln Arg Ile Asn Ser Val Lys Lys Thr Leu Thr Glu Leu Lys Ser	
	240 245 250	
	gac ttc gac aaa cat aca gat aga ttt cta agc tta gaa ggt gac aga	878
35	Asp Phe Asp Lys His Thr Asp Arg Phe Leu Ser Leu Glu Gly Asp Arg	



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	255	260	265	
	gcc aaa gtt ctg aag aca gtg act ttt gca aat gat cta aaa cca aag	926		
	Ala Lys Val Leu Lys Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys			
	270	275	280	
5	gtg tat aat cta aag aag gac ttt tcc cgt tta gaa cca tta gta aat	974		
	Val Tyr Asn Leu Lys Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn			
	285	290	295	
	gat tta aca cta cgc att ggg aga ttg gtt acc gac tta cta caa aga	1022		
	Asp Leu Thr Leu Arg Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg			
10	300	305	310	315
	gag aaa gaa att gct ttc tta agt gaa aaa ata tct aat tta aca ata	1070		
	Glu Lys Glu Ile Ala Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile			
	320	325	330	
	gtc caa gct gag att aag gat att aaa gat gaa ata gca cac att tca	1118		
15	Val Gln Ala Glu Ile Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser			
	335	340	345	
	gat atg aat tagtttgaca ttattgagat tagactaagg taattttttt aat	1170		
	Asp Met Asn			
	350			
20	gggacctctc atgagaagac tggtaaatca aaaataatga tattttggag caaaagtcac	1230		
	tttatattta atcctatttt gtacagtata aataaaactt taaaacaggt tgattttcca	1290		
	aaataaatat gctaaaacct	1310		
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35	aacacagctg gtatttcaag tctcctggga cctcactcag gaatgatacc cctcagtag	180		

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	aagcagcagg tgatcttaac tctttcaaa gagcaggcct gtctgggaag cc atg	235
	Met	
	1	
	tcc tca gca ggc aca gca acc cct ctg gaa atg gat cac aaa ctc act	283
5	Ser Ser Ala Gly Thr Ala Thr Pro Leu Glu Met Asp His Lys Leu Thr	
	5 10 15	
	tct cag cca ggc agg cca agc ttc tat tgt aac agt agg cac agt ata	331
	Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser Ile	
	20 25 30	
10	gtc gga tca tca cat cag ctg ggt ttt tgg ttt agt cat cta gag tgc	379
	Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu Ser	
	35 40 45	
	tct gga cta aag gtc ttt cag gtc tcc ttg ccc tgt gag tgc gtg aac	427
	Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val Asn	
15	50 55 60 65	
	ctc ccc acc oga att gcc tca gtt gtc ctg agc ctc atg tct ctc ctg	475
	Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu Leu	
	70 75 80	
	gtg gtg ggc cag gcc cct gca tgg gaa ggg agc ctg ctg cgg ggc agg	523
20	Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly Arg	
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	cca gct ggg ggt gct cac cta tgc gca gca tgaagttatt gaaggac	570
	Pro Ala Gly Gly Ala His Leu Cys Ala Ala	
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25	tggttggtga tggtggtgag cgtatccttc atggccagcg cgaagtgggc caggtcagcc	630
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	tgtcaggggc cgctcactgc agcagcctgc tetgctgcct tccctggcag tggtctgggg	750
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	atataatagg gccgtgggat ggtttagag gtaaacgagg atgatggtgt ttaagacca	1110
	gagcttggga ccagggtccc tacacctaat tttctctcct ggtagctgaa caaaggctca	1170
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gccacagaac acaaccatct taggcctgag ctgtgaacag caggggggttg tgtgtctgtt 1350
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    <213> Homo sapience

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15  Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu Asp
      35             40             45
    Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp Glu
      50             55             60
    Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu Gly
20  65             70             75             80
    Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu Pro
      85             90             95
    Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr Ser
      100            105            110
25  Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala His
      115            120            125
    Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val Thr
      130            135            140
    Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys Asn
30  145            150            155            160
    Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu Glu
      165            170            175
    Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala Thr
      180            185            190
35  Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu Trp

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	Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg Pro		
5	225	230	235
	Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp Met		
	245	250	255
	Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg Leu		
	260	265	270
10	Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro Lys		
	275	280	285
	Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser Glu		
	290	295	300
	Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His Phe		
15	305	310	315
	Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp Gln		
	325	330	335
	Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys Leu		
	340	345	350
20	Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly Ser		
	355	360	365
	Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met Asn		
	370	375	380
	Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn Arg		
25	385	390	395
	Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu Asn		
	405	410	415
	Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser Arg		
	420	425	430
30	Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu Glu		
	435	440	445
	Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg Glu		
	450	455	460
	Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys Val		
35	465	470	475
			480

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Lys Ala Met

&lt;210&gt; 122

&lt;211&gt; 334

5 &lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 122

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Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala Leu Ala Glu
      20          25          30
Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg Phe Trp Leu
      35          40          45
15 Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg Asp Lys Pro
      50          55          60
Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp Thr Ile Trp
      65          70          75          80
Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys Thr Ala Glu
20      85          90          95
Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro His Gly Val
      100         105         110
Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser Thr Gly Phe
      115         120         125
25 Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met Leu Thr Leu
      130         135         140
Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser Ala Gly Leu
      145         150         155         160
Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn Arg Lys Gly
30      165         170         175
Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln Glu Ala Leu
      180         185         190
Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn Arg Lys Gly
      195         200         205
35 Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val Pro Ile Phe

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 5                      245                      250                      255  
 Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr Ser Phe Gly  
 260                      265                      270  
 Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile  
 275                      280                      285  
 10      Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val Asn Gln Leu  
 290                      295                      300  
 His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu Ala His Lys  
 305                      310                      315                      320  
 Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe Cys  
 15                      325                      330  
  
 <210> 123  
 <211> 267  
 <212> PRT  
 20      <213> Homo sapience  
  
 <400> 123  
 Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly  
 1                      5                      10                      15  
 25      His Thr Val Leu Thr Trp Gly Ile Thr Leu Val Leu Phe Leu His Asp  
 20                      25                      30  
 Thr Glu Leu Arg Gln Trp Glu Glu Gln Gly Glu Leu Leu Leu Pro Leu  
 35                      40                      45  
 Thr Phe Leu Leu Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val  
 30      50                      55                      60  
 Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln Glu  
 65                      70                      75                      80  
 Glu Leu Lys Glu Glu Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu  
 85                      90                      95  
 35      Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His

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	100	105	110
	Cys Arg Glu Cys Arg Arg Cys Val Arg Arg Tyr Asp His His Cys Pro		
	115	120	125
	Trp Met Glu Asn Cys Val Gly Glu Arg Asn His Pro Leu Phe Val Val		
5	130	135	140
	Tyr Leu Ala Leu Gln Leu Val Val Leu Leu Trp Gly Leu Tyr Leu Ala		
	145	150	155
	160		
	Trp Ser Gly Leu Arg Phe Phe Gln Pro Trp Gly Leu Trp Leu Arg Ser		
	165	170	175
10	Ser Gly Leu Leu Phe Ala Thr Phe Leu Leu Leu Ser Leu Phe Ser Leu		
	180	185	190
	Val Ala Ser Leu Leu Leu Val Ser His Leu Tyr Leu Val Ala Ser Asn		
	195	200	205
	Thr Thr Thr Trp Glu Phe Ile Ser Ser His Arg Ile Ala Tyr Leu Arg		
15	210	215	220
	Gln Arg Pro Ser Asn Pro Phe Asp Arg Gly Leu Thr Arg Asn Leu Ala		
	225	230	235
	240		
	His Phe Phe Cys Gly Trp Pro Ser Gly Ser Trp Glu Thr Leu Trp Ala		
	245	250	255
20	Glu Glu Glu Glu Glu Gly Ser Ser Pro Ala Val		
	260	265	
	<210> 124		
	<211> 106		
25	<212> PRT		
	<213> Homo sapiens		
	<400> 124		
	Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro Asn Lys Val Leu		
30	1	5	10
	15		
	Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala Leu Asp Asp Pro		
	20	25	30
	Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly		
	35	40	45
35	Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser		

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50                      55                      60  
 Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met  
 65                      70                      75                      80  
 Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu  
 5                      85                      90                      95  
 Gln Asn Pro Gln Pro Met Thr Pro Pro Trp  
                     100                      105  
  
 <210> 125  
 10 <211> 224  
      <212> PRT  
      <213> Homo sapience  
  
 <400> 125  
 15 Met Thr Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro  
      1                      5                      10                      15  
 Tyr Phe Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe  
                     20                      25                      30  
 Trp Lys Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys  
 20                      35                      40                      45  
 Lys Met Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Gly Ile  
      50                      55                      60  
 Tyr Asp Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp  
      65                      70                      75                      80  
 25 Leu Ile Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu  
                     85                      90                      95  
 Tyr Lys Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile  
                     100                      105                      110  
 Met Ser Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe  
 30                      115                      120                      125  
 Asp Trp Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val  
      130                      135                      140  
 His Tyr Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp  
      145                      150                      155                      160  
 35 Leu Tyr His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser



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165 170 175  
 Val Tyr Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu  
 180 185 190  
 Gly Ser Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu  
 5 195 200 205  
 Ala Leu Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser  
 210 215 220  
  
 <210> 126  
 10 <211> 258  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 126  
 15 Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val Tyr Ser Val Pro Arg  
 1 5 10 15  
 Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu Leu Ser Ala Leu Leu  
 20 25 30  
 Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro Pro Leu Cys His Gly  
 20 35 40 45  
 Leu Pro Thr Gln Arg Glu Asp Gly Asn Pro Cys Asp Phe Asp Trp Arg  
 50 55 60  
 Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile Val Met Met Lys Asn  
 65 70 75 80  
 25 Arg Arg Ser Met Phe Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly  
 85 90 95  
 Pro Glu Tyr Ile Lys Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu  
 100 105 110  
 Glu Arg Asp Lys Arg Val Thr Trp Ile Val Glu Phe Phe Ala Asn Trp  
 30 115 120 125  
 Ser Asn Asp Cys Gln Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu  
 130 135 140  
 Lys Tyr Asn Cys Thr Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg  
 145 150 155 160  
 35 Tyr Thr Asp Val Ser Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr

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165 170 175  
 Lys Gln Leu Pro Thr Leu Ile Leu Phe Gln Gly Gly Lys Glu Ala Met  
 180 185 190  
 Arg Arg Pro Gln Ile Asp Lys Lys Gly Arg Ala Val Ser Trp Thr Phe  
 5 195 200 205  
 Ser Glu Glu Asn Val Ile Arg Glu Phe Asn Leu Asn Glu Leu Tyr Gln  
 210 215 220  
 Arg Ala Lys Lys Leu Ser Lys Ala Gly Asp Asn Ile Pro Glu Glu Gln  
 225 230 235 240  
 10 Pro Val Ala Ser Thr Pro Thr Thr Val Ser Asp Gly Glu Asn Lys Lys  
 245 250 255  
 Asp Lys  
  
 <210> 127  
 15 <211> 110  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 127  
 20 Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro Pro Phe Ile Ser Glu  
 1 5 10 15  
 Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp Tyr Cys Arg Thr Ser  
 20 25 30  
 Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile Leu Gly Leu Thr Gly  
 25 35 40 45  
 Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser Val Leu Leu Ser Leu  
 50 55 60  
 Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn Lys Tyr Phe Lys Ser  
 65 70 75 80  
 30 Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly Gly Leu Phe Thr Tyr  
 85 90 95  
 Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val His Val Tyr  
 100 105 110  
  
 35 <210> 129

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<211> 91  
 <212> PRT  
 <213> Homo sapiens

5 <400> 128  
 Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser Gln Ser  
 1 5 10 15  
 Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile Ala Glu  
 20 25 30  
 10 Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val Lys Lys  
 35 40 45  
 Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp Gly Arg  
 50 55 60  
 Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn His Leu  
 15 65 70 75 80  
 Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly  
 85 90

<210> 129  
 20 <211> 344  
 <212> PRT  
 <213> Homo sapiens

<400> 129  
 25 Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser  
 1 5 10 15  
 Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu  
 20 25 30  
 Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val  
 30 35 40 45  
 Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys  
 50 55 60  
 Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe  
 65 70 75 80  
 35 Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu

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	85	90	95
	Leu Gly Ser Trp Val Leu Ser Ala	Leu Phe Asp Phe Leu Leu Ile Glu	
	100	105	110
5	Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser		
	115	120	125
	Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser		
	130	135	140
	Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr		
	145	150	155
10	Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly		
	165	170	175
	Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys		
	180	185	190
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser		
15	195	200	205
	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser		
	210	215	220
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp		
	225	230	235
20	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe		
	245	250	255
	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Gly Met		
	260	265	270
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val		
25	275	280	285
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu		
	290	295	300
	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg		
	305	310	315
30	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val		
	325	330	335
	Ala Thr Asn Phe Leu Leu Gln His		
	340		
35	<210> 130		

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&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

5 &lt;400&gt; 130

Met Gly Pro Pro Pro Gly Ala Gly Val Ser Cys Arg Gly Gly Cys Gly  
 1 5 10 15  
 Phe Ser Arg Leu Leu Ala Trp Cys Phe Leu Leu Ala Leu Ser Pro Gln  
 20 25 30  
 10 Ala Pro Gly Ser Arg Gly Ala Glu Ala Val Trp Thr Ala Tyr Leu Asn  
 35 40 45  
 Val Ser Trp Arg Val Pro His Thr Gly Val Asn Arg Thr Val Trp Glu  
 50 55 60  
 Leu Ser Glu Glu Gly Val Tyr Gly Gln Asp Ser Pro Leu Glu Pro Val  
 15 65 70 75 80  
 Ala Gly Val Leu Val Pro Pro Asp Gly Pro Gly Ala Leu Asn Ala Cys  
 85 90 95  
 Asn Pro His Thr Asn Phe Thr Val Pro Thr Val Trp Gly Ser Thr Val  
 100 105 110  
 20 Gln Val Ser Trp Leu Ala Leu Ile Gln Arg Gly Gly Gly Cys Thr Phe  
 115 120 125  
 Ala Asp Lys Ile His Leu Ala Tyr Glu Arg Gly Ala Ser Gly Ala Val  
 130 135 140  
 Ile Phe Asn Phe Pro Gly Thr Arg Asn Glu Val Ile Pro Met Ser His  
 145 150 155 160  
 25 Pro Gly Ala Val Asp Ile Val Ala Ile Met Ile Gly Asn Leu Lys Gly  
 165 170 175  
 Thr Lys Ile Leu Gln Ser Ile Gln Arg Gly Ile Gln Val Thr Met Val  
 180 185 190  
 30 Ile Glu Val Gly Lys Lys His Gly Pro Trp Val Asn His Tyr Ser Ile  
 195 200 205  
 Phe Phe Val Ser Val Ser Phe Phe Ile Ile Thr Ala Ala Thr Val Gly  
 210 215 220  
 Tyr Phe Ile Phe Tyr Ser Ala Arg Arg Leu Arg Asn Ala Arg Ala Gln  
 35 225 230 235 240

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	Ser Arg Lys Gln Arg Gln Leu Lys Ala Asp Ala Lys Lys Ala Ile Gly	
	245	250 255
	Arg Leu Gln Leu Arg Thr Leu Lys Gln Gly Asp Lys Glu Ile Gly Pro	
	260	265 270
5	Asp Gly Asp Ser Cys Ala Val Cys Ile Glu Leu Tyr Lys Pro Asn Asp	
	275	280 285
	Leu Val Arg Ile Leu Thr Cys Asn His Ile Phe His Lys Thr Cys Val	
	290	295 300
	Asp Pro Trp Leu Leu Glu His Arg Thr Cys Pro Met Cys Lys Cys Asp	
10	305	310 315 320
	Ile Leu Lys Ala Leu Gly Ile Glu Val Asp Val Glu Asp Gly Ser Val	
	325	330 335
	Ser Leu Gln Val Pro Val Ser Asn Glu Ile Ser Asn Ser Ala Ser Ser	
	340	345 350
15	His Glu Glu Asp Asn Arg Ser Glu Thr Ala Ser Ser Gly Tyr Ala Ser	
	355	360 365
	Val Gln Gly Thr Asp Glu Pro Pro Leu Glu Glu His Val Gln Ser Thr	
	370	375 380
	Asn Glu Ser Leu Gln Leu Val Asn His Glu Ala Asn Ser Val Ala Val	
20	385	390 395 400
	Asp Val Ile Pro His Val Asp Asn Pro Thr Phe Glu Glu Asp Glu Thr	
	405	410 415
	Pro Asn Gln Glu Thr Ala Val Arg Glu Ile Lys Ser	
	420	425
25		
	<210> 131	
	<211> 1449	
	<212> DNA	
	<213> Homo sapience	
30		
	<400> 131	
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	aagtttgatg atttttgagga tgaggaggac atagtagagt atgatgataa tgacttgcgt	120
	gaatttgagg atgtcatgga agactctgtt actgaatctc ctcaacgggt cataatcact	180
35	gaagatgatg aagatgagac cactgtggag ttggaagggc aggatgaaaa ccaagaagga	240

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	gattttgaag atgcagatac ccaggagggga gatactgaga gtgaaccata tgaatgatgaa	300
	gaatttgaag gttatgaaga caaaccagat acttcttcta gcaaaaataa agacccaata	360
	acgattgttg atgttctctgc acacctocag aacagctggg agagtatta tctagaaatt	420
	ttgatggga ctggtctctgc tcttatata atgaattaca tcattgggaa gaataaaac	480
5	agtcgcttg cacagggctg gtttaacact catagggagc ttttggagag caactttact	540
	ttagtgggg atgatggaac taacaaagaa gccacaagca caggaaagtt gaaccaggag	600
	aatgagcaca tctataacct gtggtgttct ggtcagagtgt gctgtgaggg catgcttacc	660
	cagctgaggt tctcaagag acaagactta ctgaatgtcc tggcccggt gatgaggcca	720
	gtgagtgatc aagtgcacat aaaagtaacc atgaatgatg aagacatgga tacctacgta	780
10	tttctgttg gcacacggaa agccttggtg cgactacaga aagagatgca ggatttgagt	840
	gagttttgta gtgataaacc taagtctgga gcaagtatg gactgccgga ctctttggcc	900
	atcctgtcag agatgggaga agtcacagac ggaatgatgg atacaagat ggttcaactt	960
	cttacacact atgctgaca gattgaatct gttcattttt cagaccagtt ctctgggtcca	1020
	aaaaatatgc aagaggaagg tcaagcctta aagctacctg acactaagag gacactgttg	1080
15	tttacattta atgtgcctgg ctcaggtaac acttaccctaa aggatattgga ggcaactgta	1140
	ccctgtatga acatggtgat ttattctatt gataaagcca aaaagttccg actcaacaga	1200
	gaagggcaac aaaaagcaga taagaaccgt gcccgagtag aagagaactt cttgaactg	1260
	acacatgtgc aaagacagga agcagcacag tctggcgagg aggagaaaaa aagagcagag	1320
	aaggagcgaa tcatgaatga ggaagatcct gagaacacgc gcaggctgga ggaggctgca	1380
20	ttgaggcgtg agcaaaagaa gttggaaaaa aagcaaatga aaatgaaca aatcaaatg	1440
	aaagccatg	1449
	<210> 132	
	<211> 1002	
25	<212> DNA	
	<213> Homo sapiens	
	<400> 132	
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30	ctacagtttg tcttctctct cttggcactg gccagatct gcaactgtggg cttcatagcc	120
	ctcctgttta caagattctg gctcctcact gtctgtatg cggcctggtg gtatctggac	180
	cgagacaagc cacggcaggg gggccggcac atccaggcca tcaggctctg gactatatgg	240
	aagtacatga aggaactatt ccccatctcg ctggtcaaga ctgctgagct ggacccctct	300
	cggaaactaca ttgcgggctt ccaaccccat ggagtcctgg cagtcggagc ctttgcacac	360
35	ctgtgcactg agagcacagg cttctctctg atcttcccg gtatccggcc ccatctgatg	420

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atgctgacct tgtggttccg ggcaccttc ttcagagatt acatcatgtc tgcagggttg 480  
 gtcacatcag aaaaggagag tgctgctcac attctgaaca ggaagggttg cggaaacttg 540  
 ctgggcatca ttgtaggggg tgcacaggag gccctggatg ccaggcctgg atccttcacg 600  
 ctgttactgc ggaaccgaaa gggttctgtc aggtctgccc tgacacacgg ggcacctctg 660  
 5 gtgcaatct tctccttcgg ggagaatgac ctatttgacc agattcccaa ctcttttggc 720  
 tcttggttac gctatatcca gaatcggttg cagaagatca tgggcatctc cctcccaactc 780  
 ttctatggcc gtggtgtctt ccagtacagc tttggtttaa taccctacgg ccggcccatc 840  
 accactgtgg tgggggaagg catcgaggta cagaagacgc tgcctccctc ggaggaggag 900  
 gtgaaccagc tgcaccagcg ttatatcaaa gagctgtgca acctcttcga ggcccacaaa 960  
 10 cttaagtcca acatccctgc tgaccagcac ttggagttct gc 1002

&lt;210&gt; 133

&lt;211&gt; 801

&lt;212&gt; DNA

15 &lt;213&gt; Homo sapiens

&lt;400&gt; 133

atggcgccct gggcgctccc cagccctggg gtcttggtgc ggaacgggca caccgtgctg 60  
 acctggggaa tcacgtggtt gctcttctg caagataccg agctggggca atgggaggag 120  
 20 cagggggagc tgctcctgac cctcacttc ctgctcctgg tgctgggctc cctgctgctc 180  
 taactgctg tgctcactat ggacctggc taagtgaatg tgcagcccca gctcaggag 240  
 gagctcaaa agggagcagc agccatggtt cctccagcca tccctctctg gcgtgcaga 300  
 taactgctgg tgctgcagcc cctgagggtt cgggactgac gtgagtgcg ccgttgctgc 360  
 cgcgctacg accaccactg cccctggatg gagaactgtg tgggagagcg caaccacca 420  
 25 ctctttgtgg tctacctggc gctgcagctg gtggtgcttc tgggggct gtacctgga 480  
 tggtcaggcc tccgggtctt ccagccctgg ggtctgtggt tgcggctcag cgggtcctg 540  
 ttgcacacct tctgtgtgt gtccctcttc tegtgtgtg ccagctgct cctgctctg 600  
 caactctacc tggtyggcag caaccacc accctgggaa tcatctctc acaccgctc 660  
 gcttatctcc gccagcgccc cagcaacccc ttcgaccgag gctgacccg caacctggc 720  
 30 cactctctct gtggatggc ctcagggtcc tgggagaccc tctgggctga ggaggaggaa 780  
 gagggcagca gccagctgt t 801

&lt;210&gt; 134

&lt;211&gt; 318

35 &lt;212&gt; DNA



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&lt;213&gt; Homo sapiens

&lt;400&gt; 134

5 atgtccacta acaatatgtc ggacccacgg aggcogaaca aagtgtgag gtacaagccc 60  
 ccgccgagcg aatgtaaccc ggccttgagc gacccgacgc cggactacat gaacctgtcg 120  
 ggcatgaccc tcagcatgtg cggcctcatg ctttaagctga agtgggtgtg ttgggtcgct 180  
 gtctactgct ccttcacagc ctttgccaac tctcggagct cggaggacac gaagcaaatg 240  
 atgagtagct tcattgtgtc catctctgcc gtggtgatgt cctatctgca gaatcctcag 300  
 cccatgacgc ccccatgg 318

10

&lt;210&gt; 135

&lt;211&gt; 672

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

15

&lt;400&gt; 135

20 atgacctgt ttcacttcgg gaactgcttc gctcttgctt acttcccta ctteatcacc 60  
 tacaagtcca gggcctgtc cgagtacaac gccttctgga aatgcgtcca ggctggagtc 120  
 acctacctct ttgtccaaact ctgcaagatg ctgttcttgg ccactttctt tcccactcgg 180  
 gaaggcggca tctatgaact cattggggag ttcattgaagg ccagcgtgga tgtggcagac 240  
 ctgataggtc taaaccttgt catgtcccg aatgcggcca agggagagta caagatcatg 300  
 gttgctgccc tgggtggggc caactgctgag cttattatgt cccgctgcat tcccctatgg 360  
 gtcggagccc ggggcattga gtttgactgg aagtacatcc agatgagcat agactccaac 420  
 atcagctctg tccattacat cgtcgcgtct gctcaggtct ggatgataac acgctatgat 480  
 25 ctgtaccaca ccttccggcc agctgtcttc ctgctgatgt tcctcagtg ctacaaggcc 540  
 tttgttatgg agaccttcgt ccacctctgc tcgctgggca gttgggcagc tctactggcc 600  
 cgagcagtg taacggggct gctggccctc agcaactttg ccctgtatgt cgcgctgtgc 660  
 aatgtgaact cc 672

30

&lt;210&gt; 136

&lt;211&gt; 774

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

35

&lt;400&gt; 136

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	atggcggtct tggcactct aattgetctc gtgtattcgg tgcgcgact ttcacgatgg	60
	ctcgcccaac cttactacct tetgtcgccc ctgtctctg ctgccttctt actcgtgagg	120
	aaactgccc cgtcttgcca cggctctgcc acccaacgcg aagacggtaa cccgtgtgac	180
	tttgactgga gagaagtgga gatacctgat tttctcagtg ccattgtgat gatgaagaac	240
5	cgcagatcca tgttctctga- gacgtgcata cccccctat atatggggcc tgagtatac	300
	aagtacttca atgataaac cattgatgag gaactagaac gggacaagag ggtcacttgg	360
	attgtggagt tctttgcaa ttggtctaat gactgccaat catttgccc tatctatgct	420
	gacctctccc ttaaatacaa ctgtacaggg cttaaatttg ggaagggtgga tgttggacgc	480
	tatactgatg ttagtaacgc gtacaaagtg agcacatcac cctcaccac gcaactccct	540
10	acctgatcc tgttccaaag tggcaaggag gcaatgcggc ggcacagat tgacaagaaa	600
	ggacgggctg tctcatggac cttctctgag gagaatgtga tccgagaatt taacttaaat	660
	gagctatacc agcggggcaa gaaactatca aaggctggag acaatatccc tgaggagcag	720
	cctgtggctt caacccccac cacagtgtca gatggggaaa acaagaagga taaa	774
15	<210> 137	
	<211> 330	
	<212> DNA	
	<213> Homo sapience	
20	<400> 137	
	atggccgcgg tggtagccaa gggggaaggg cggccgttca tcagcgagge ggcctgccc	60
	ggcaacgcgg cgttcctgga ttattgcgg acccgggtgt cagcgctgtc gggggccacg	120
	gccggcatcc tcggcctcac cggcctctac ggttctatct tctacctgct cgcctcgtc	180
	ctgtctctcc tgcctctcat tctcaaggcg ggaaggaggt ggaacaaata ttccaatca	240
25	cggagacctc tctttacagg aggcctcatc gggggcctct tcacctacgt cctgttctgg	300
	acgttctctt acggcatggt gcacgtctac	330
	<210> 138	
	<211> 273	
30	<212> DNA	
	<213> Homo sapience	
	<400> 138	
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ctgttcagc aagatgtgaa aaaaagaaga agctatggaa actcatctga ttccagatat 180
gatgatggaa gagggccacc aggaaaccct ccccgaaaga tgggtagaat caatcatctg 240
cgtggcccta gtcccccctc aatggctggg gga 273

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 tttgtgtatg accttcacgc agtcaagaac gacttccaga tttggaggtt gatatgtgga 180  
 agaataatctt gccttgattt gaaagatact ttctgcagta gtctgcttat ttataatctt 240  
 15 aggatatttg aaagaagata tgggaagcaga aaatttgcac ccttttctgt ggggttcctgg 300  
 gttttgtcag ccttatttga cttctcctcc attgaagcta tgcagtattt ctttggcctc 360  
 actgcagcta gtaatttgcc ttctggatto ctggcacctg tgtttgtctt gtttgacca 420  
 ttttactgct ccataccaag agtcccaagt gcacaaatto tgggtccgtt gtccatcaca 480  
 aacaagacat tgatttatat attgggaactg cagcttttca cctctggttc ctacatctgg 540  
 20 attgtagcca taagtggact tatgtccggt ctgtgtctacg acagcaaaat gttccaggtg 600  
 catcaggtgc tctgcacccc cagctggatg gcaaaattct tttttggac aactgaacct 660  
 atcttctctt cttcagaacc caccagcgaa gccagaattg ggatgggagc cagctggac 720  
 atccagagac agcagagaat ggagctgctg gacgggcagc tgatgttctc tcagtttgca 780  
 caaggagggc gacagagaca gcagcaggga ggaatgatca attggaatcg tcttttccct 840  
 25 cctttacgct agcgacaaaa cgtaaactat caggcggtc ggcagtctga gccagcagcg 900  
 cccctctag aagtttctga ggaacaggct gcccggtc tggagatggg attttcaga 960  
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35 <400> 140

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	gcagtgtgga ccgcgtacct caacgtgtcc tggcgggttc cgcacacggg agtgaaccgt	180
	acggtgtggg agctgagcga ggaggcgtg tacggccaag actcgccgc ggagcctgtg	240
5	gctggggtcc tggtagccgc cgaaggggcc ggggcgctta acgctgtaa cccgcacacg	300
	aatttcacgg tgcccacggt ttggggaagc accgtgcag tctcttgggt ggccctcacc	360
	caacgcggcg ggggctgcac cttcgagac aagatccacc tggcttatga gagaggggcg	420
	tctggagccg tcatctttaa cttccccggg acccgcaatg aggtcatccc catgtctcac	480
	ccgggtgcag tagacattgt tgcaatcatg atcggcaatc tgaaggcac aaaaattctg	540
10	caatctattc aaagaggcat acaagtaca atggtcatag aagtaggaa aaaacatggc	600
	ccttgggtga atcactatc aatttttttc gttctgtgt ctttttttat tattacggcg	660
	gcaactgtgg gctattttat cttttattct gctgaaggc tacggaatgc aagagctcaa	720
	agcagggaagc agaggcaatt aaaggcagat gctaaaaaag ctattggaa gcttcaacta	780
	cgcacactga aacaaggaga caaggaaatt ggccctgatg gagatagttg tgcgtgtgc	840
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	aagacatgtg ttgaccatg gctgttagaa cacaggactt gcccatgtg caaatgtgac	960
	atactcaaag ctttgggaat tgaggtggat gttgaagatg gatcagtgtc tttaacaagtc	1020
	cctgtatcca atgaaatata taatagtgc tctccccatg aagaggataa tcgcagcgag	1080
	accgcatcat ctggatatgc ttcagtacag ggaacagatg aaccgcctct ggagggaacac	1140
20	gtgcagtcac caaatgaaag tctacagctg gtaaaccatg aagcaaatte tgtggcagt	1200
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	actgctgttc gagaaattaa atct	1284
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	<213> Homo sapiens	
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35	a atg aaa gcc ttc cag act ttc tgt gtt gtc ctt ctg gtg ttt ggg	166

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		Ser	Val	Ser	Glu	Ala	Lys	Phe	Asp	Asp	Phe	Glu	Asp	Glu	Glu	Asp	Ile
5							20					25				30	
		gta	gag	tat	gat	gat	aat	gac	ttc	gct	gaa	ttt	gag	gat	gtc	atg	gaa
		Val	Glu	Tyr	Asp	Asp	Asn	Asp	Phe	Ala	Glu	Phe	Glu	Asp	Val	Met	Glu
							35					40				45	
		gac	tct	gtt	act	gaa	tct	cct	caa	cgg	gtc	ata	atc	act	gaa	gat	gat
10		Asp	Ser	Val	Thr	Glu	Ser	Pro	Gln	Arg	Val	Ile	Ile	Thr	Glu	Asp	Asp
							50					55				60	
		gaa	gat	gag	acc	act	ctg	gag	ttg	gaa	ggg	cag	gat	gaa	aac	caa	gaa
		Glu	Asp	Glu	Thr	Thr	Val	Glu	Leu	Glu	Gly	Gln	Asp	Glu	Asn	Gln	Glu
							65					70				75	
15		gga	gat	ttt	gaa	gat	gca	gat	acc	cag	gag	gga	gat	act	gag	agt	gaa
		Gly	Asp	Phe	Glu	Asp	Ala	Asp	Thr	Gln	Glu	Gly	Asp	Thr	Glu	Ser	Glu
							80					85				90	
		cca	tat	gat	gat	gaa	gaa	ttt	gaa	ggt	tat	gaa	gac	aaa	cca	gat	act
		Pro	Tyr	Asp	Asp	Glu	Glu	Phe	Glu	Gly	Tyr	Glu	Asp	Lys	Pro	Asp	Thr
20							100					105				110	
		tct	tct	agc	aaa	aat	aaa	gac	cca	ata	acg	att	gtt	gat	gtt	cct	gca
		Ser	Ser	Ser	Lys	Asn	Lys	Asp	Pro	Ile	Thr	Ile	Val	Asp	Val	Pro	Ala
							115					120				125	
		cac	ctc	cag	aac	agc	tgg	gag	agt	tat	tat	cta	gaa	att	ttg	atg	gtg
25		His	Leu	Gln	Asn	Ser	Trp	Glu	Ser	Tyr	Tyr	Leu	Glu	Ile	Leu	Met	Val
							130					135				140	
		act	ggt	ctg	ctt	gct	tat	atc	atg	aat	tac	atc	att	ggg	aag	aat	aaa
		Thr	Gly	Leu	Leu	Ala	Tyr	Ile	Met	Asn	Tyr	Ile	Ile	Gly	Lys	Asn	Lys
							145					150				155	
30		aac	agt	cgc	ctt	gca	cag	gcc	tgg	ttt	aac	act	cat	agg	gag	ctt	ttg
		Asn	Ser	Arg	Leu	Ala	Gln	Ala	Trp	Phe	Asn	Thr	His	Arg	Glu	Leu	Leu
							160					165				170	
		gag	agc	aac	ttt	act	tta	gtg	ggg	gat	gat	gga	act	aac	aaa	gaa	gcc
		Glu	Ser	Asn	Phe	Thr	Leu	Val	Gly	Asp	Asp	Gly	Thr	Asn	Lys	Glu	Ala
35							180					185				190	

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	Thr Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu	
	195 200 205	
	tgg tgt tct ggc cga gtg tgc tgt gag ggc atg ctt atc cag ctg agg	790
5	Trp Cys Ser Gly Arg Val Cys Cys Glu Gly Met Leu Ile Gln Leu Arg	
	210 215 220	
	ttc ctc aag aga caa gac tta ctg aat gtc ctg gcc cgg atg atg agg	838
	Phe Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg	
	225 230 235	
10	cca gtg agt gat caa gtg caa ata aaa gta acc atg aat gat gaa gac	886
	Pro Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp	
	240 245 250 255	
	atg gat acc tac gta ttt gct gtt ggc aca cgg aaa gcc ttg gtg cga	934
	Met Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg	
15	260 265 270	
	cta cag aaa gag atg cag gat ttg agt gag ttt tgt agt gat aaa cct	982
	Leu Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro	
	275 280 285	
	aag tct gga gca aag tat gga ctg ccg gac tct ttg gcc atc ctg tca	1030
20	Lys Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser	
	290 295 300	
	gag atg gga gaa gtc aca gac gga atg atg gat aca aag atg gtt cac	1078
	Glu Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His	
	305 310 315	
25	ttt ctt aca cac tat gct gac aag att gaa tct gtt cat ttt tca gac	1126
	Phe Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp	
	320 325 330 335	
	cag ttc tct ggt cca aaa att atg caa gag gaa ggt cag cct tta aag	1174
	Gln Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys	
30	340 345 350	
	cta cct gac act aag agg aca ctg ttg ttt aca ttt aat gtg cct ggc	1222
	Leu Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly	
	355 360 365	
	tca ggt aac act tac cca aag gat atg gag gca ctg cta ccc ctg atg	1270
35	Ser Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met	

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	370	375	380	
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	Asn Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn			
	385	390	395	
5	aga gaa ggc aaa caa aaa gca gat aag aac cgt gcc cga gta gaa gag	1366		
	Arg Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu			
	400	405	410	415
	aac ttc ttg aaa ctg aca cat gtg caa aga cag gaa gca gca cag tct	1414		
	Asn Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser			
10	420	425	430	
	cgg cgg gag gag aaa aaa aga gca gag aag gag cga atc atg aat gag	1462		
	Arg Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu			
	435	440	445	
	gaa gat cct gag aaa cag cgc agg ctg gag gag gct gca ttg agg cgt	1510		
15	Glu Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg			
	450	455	460	
	gag caa aag aag ttg gaa aag aag caa atg aaa atg aaa caa atc aaa	1558		
	Glu Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys			
	465	470	475	
20	gtg aaa gcc atg taaagccatc ccagagattt gagttctgat gccacctgta	1610		
	Val Lys Ala Met			
	480			
	agctctgaat tcacaggaaa catgaaaaac gccagtcctat ttctcaacct taaatttcag	1670		
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	atatattttaa aattataata caaatcatca gtgcttttag tacttcagtg tttaaagaaa	1910		
	taccatgaaa tttataggta gataaccaga ttgttgcttt ttgtttaaac caagcagttg	1970		
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30	ataaacattg cttgatgttt	2050		
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35	<213> Homo sapiens			

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&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (70)...(1074)

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 Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg  
 1 5 10

10 agg ctg cag aca ctt gct gtc cta cag ttt gtc ttc tcc ttc ttg gca 156  
 Arg Leu Gln Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala  
 15 20 25  
 ctg gcc gag atc tgc act gtg ggc ttc ata gcc ctc ctg ttt aca aga 204  
 Leu Ala Glu Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg

15 30 35 40 45  
 ttc tgg ctc ctc act gtc ctg tat gcg gcc tgg tgg tat ctg gac cga 252  
 Phe Trp Leu Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg  
 50 55 60  
 gac aag cca cgg cag ggg ggc cgg cac atc cag gcc atc agg tgc tgg 300  
 Asp Lys Pro Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp

20 65 70 75  
 act ata tgg aag tac atg aag gac tat ttc ccc atc tcg ctg gtc aag 348  
 Thr Ile Trp Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys  
 80 85 90

25 act gct gag ctg gac ccc tct cgg aac tac att gcg ggc ttc cac ccc 396  
 Thr Ala Glu Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro  
 95 100 105  
 cat gga gtc ctg gca gtc gga gcc ttt gcc aac ctg tgc act gag agc 444  
 His Gly Val Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser

30 110 115 120 125  
 aca ggc ttc tct tcg atc ttc ccc ggt atc cgc ccc cat ctg atg atg 492  
 Thr Gly Phe Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met  
 130 135 140  
 ctg acc ttg tgg ttc cgg gcc ccc ttc ttc aga gat tac atc atg tct 540

35 Leu Thr Leu Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser



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	145	150	155	
	gca ggg ttg gtc aca tca gaa aag gag agt gct gct cac att ctg aac	588		
	Ala Gly Leu Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn			
	160	165	170	
5	agg aag ggt ggc gga aac ttg ctg ggc atc att gta ggg ggt gcc cag	636		
	Arg Lys Gly Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln			
	175	180	185	
	gag gcc ctg gat gcc agg cct gga tcc ttc acg ctg tta ctg cgg aac	684		
	Glu Ala Leu Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn			
10	190	195	200	205
	cga aag ggc ttc gtc agg ctc gcc ctg aca cac ggg gca ccc ctg gtg	732		
	Arg Lys Gly Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val			
	210	215	220	
	cca atc ttc tcc ttc ggg gag aat gac cta ttt gac cag att ccc aac	780		
15	Pro Ile Phe Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn			
	225	230	235	
	tct tct ggc tcc tgg tta cgc tat atc cag aat cgg ttg cag aag atc	828		
	Ser Ser Gly Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile			
	240	245	250	
20	atg ggc atc tcc ctc cca ctc ttt cat gcc cgt ggt gtc ttc cag tac	876		
	Met Gly Ile Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr			
	255	260	265	
	agc ttt ggt tta ata ccc tac cgc cgg ccc atc acc act gtg gtg ggg	924		
	Ser Phe Gly Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly			
25	270	275	280	285
	aag ccc atc gag gta cag aag acg ctg cat ccc tcg gag gag gag gtg	972		
	Lys Pro Ile Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val			
	290	295	300	
	aac cag ctg cac cag cgt tat atc aaa gag ctg tgc aac ctc ttc gag	1020		
30	Asn Gln Leu His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu			
	305	310	315	
	gcc cac aaa ctt aag ttc aac atc cct gct gac cag cac ttg gag ttc	1068		
	Ala His Lys Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe			
	320	325	330	
35	tgc tgagcccaa agggcagggc caacattagg gagcccagca ggaggtgctg	1120		

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Cys

	tgctgagaag	acttcctgga	ggtgtttgtt	gaacatatct	gcagagcctt	cccagactcc	1180
	tgcaaatcca	acccatatca	ggctgtaagt	cagagcaggc	aatgcagaag	aggagaccag	1240
	accaaggggt	cagctggggc	taggacagt	agggctgcta	gaggggctgg	gcctctcttt	1300
5	gcacatggac	actgggccc	tctctatatt	gagtggctct	ttaacattca	ttggtggctg	1360
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	gcctctcttc	tactgcattc	tgttggtcga	agcaagtcac	aacccagcag	attcaaggag	1480
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10	aaaagcctga	agcacazyca	ctctccccc	caggcacaca	caccttgaa	ttcctgtgt	1660
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	cacaaagctg	accgcgccat	ttctactca	gcctcctcc	atgacctcc	attgctccta	1840
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	ggcctggaag	gatgaatgga	agcagcagtt	cctgaaccag	gaagactcat	gtgtgggggc	2020
	cattgctggg	caagggggac	gaacaggctt	ggtgacctct	caagggaggga	gcagggagca	2080
	agcattccca	cttcaccttc	ctccattcag	tctgtgcca	agttccccac	tgctgagcc	2140
	caactagaag	ctggaggagg	ggaggggcct	tggtgcagt	ccaggcatgt	aggcctcctg	2200
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	ccagcctgct	catectcctc	tctcttctc	ccttactccg	tgtccctcc	actcggaacc	2380
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	gatgcctagg	aatgccatat	cctccccatt	atctccccct	tgtctggata	attcctaact	2500
25	atcctacaat	actgatttta	tctgtgcana	gaagtcttcc	ccagtgcctc	tggttgacag	2560
	gggtttctc	tggcttctcc	agactttctg	ttctccacc	acagccctta	gcacctggg	2620
	gaggagggtg	tgtgtccag	gtaaatgctg	cgcgaatgcc	cctgcctcta	gtgcactccc	2680
	tccagcctac	ccacaaacag	gacctgcctc	ctgtctcaca	aataaaaactg	aactcttgaa	2740
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30	<210> 143						
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	<212> DNA						
	<213> Homo sapience						
35	<220>						

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&lt;221&gt; CDS

&lt;222&gt; (32)...(835)

&lt;400&gt; 143

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	Met Ala Pro Trp Ala Leu Leu	
	1 5	
	agc cct ggg gtc ctg gtg cgg acc ggg cac acc gtg ctg acc tgg gga	100
	Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly	
10	10 15 20	
	atc acg ctg gtg ctc ttc ctg cac gat acc gag ctg cgg caa tgg gag	148
	Ile Thr Leu Val Leu Phe Leu His Asp Thr Glu Leu Arg Gln Trp Glu	
	25 30 35	
	gag cag ggg gag ctg ctc ctg ccc ctc acc ttc ctg ctc ctg gtg ctg	196
15	Glu Gln Gly Glu Leu Leu Leu Pro Leu Thr Phe Leu Leu Val Leu	
	40 45 50 55	
	ggc tcc ctg ctg ctc tac ctc gct gtg tca ctc atg gac cct ggc tac	244
	Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr	
	60 65 70	
20	gtg aat gtg cag ccc cag cct cag gag gag ctc aaa gag gag cag aca	292
	Val Asn Val Gln Pro Gln Pro Gln Glu Glu Leu Lys Glu Glu Gln Thr	
	75 80 85	
	ggc atg gtt cct cca gcc atc cct ctt cgg cgc tgc aga tac tgc ctg	340
	Ala Met Val Pro Pro Ala Ile Pro Leu Arg Arg Cys Arg Tyr Cys Leu	
25	90 95 100	
	gtg ctg cag ccc ctg agg gct cgg cac tgc cgt gag tgc cgc cgt tgc	388
	Val Leu Gln Pro Leu Arg Ala Arg His Cys Arg Glu Cys Arg Arg Cys	
	105 110 115	
	gtc cgc cgc tac gac cac cac tgc ccc tgg atg gag aac tgt gtg gga	436
30	Val Arg Arg Tyr Asp His His Cys Pro Trp Met Glu Asn Cys Val Gly	
	120 125 130 135	
	gag cgc aac cac cca ctc ttt gtg gtc tac ctg gcg ctg cag ctg gtg	484
	Glu Arg Asn His Pro Leu Phe Val Val Tyr Leu Ala Leu Gln Leu Val	
	140 145 150	
35	gtg ctt ctg tgg ggc ctg tac ctg gca tgg tca ggc ctc cgg ttc ttc	532

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	Val Leu Leu Trp Gly Leu Tyr Leu Ala Trp Ser Gly Leu Arg Phe Phe	
	155 160 165	
	cag ccc tgg ggt ctg tgg ttg cgg tcc agc ggg ctc ctg ttc gcc acc	580
	Gln Pro Trp Gly Leu Trp Leu Arg Ser Ser Gly Leu Leu Phe Ala Thr	
5	170 175 180	
	ttc ctg ctg ctg tcc ctc ttc tgg ttg gtg gcc agc ctg ctc ctc gtc	628
	Phe Leu Leu Leu Ser Leu Phe Ser Leu Val Ala Ser Leu Leu Leu Val	
	185 190 195	
	tgg cac ctc tac ctg gtg gcc agc aac acc acc acc tgg gaa ttc atc	676
10	Ser His Leu Tyr Leu Val Ala Ser Asn Thr Thr Thr Trp Glu Phe Ile	
	200 205 210 215	
	tcc tca cac cgc atc gcc tat ctc cgc cag cgc ccc agc aac ccc ttc	724
	Ser Ser His Arg Ile Ala Tyr Leu Arg Gln Arg Pro Ser Asn Pro Phe	
	220 225 230	
15	gac cga ggc ctg acc cgc aac ctg gcc cac ttc ttc tgt gga tgg ccc	772
	Asp Arg Gly Leu Thr Arg Asn Leu Ala His Phe Phe Cys Gly Trp Pro	
	235 240 245	
	tca ggg tcc tgg gag acc ctc tgg gct gag gag gag gaa gag ggc agc	820
	Ser Gly Ser Trp Glu Thr Leu Trp Ala Glu Glu Glu Glu Glu Gly Ser	
20	250 255 260	
	agc cca gct gtt taggggtgct ggaggccggg ctacogtett gtgcctga	870
	Ser Pro Ala Val	
	265	
	aaaccacggg gccctgtccc agctgggggtg agcgcctcaga gggcctgggg ccctcactcc	930
25	tgccacagcc tccagagccc cagaacggag cttcaagtca gacagatccc tgccttggtg	990
	ggcagttctg ccttccaagg aagaagggga agaaaaggac ctgtgggttg ctcaggccca	1050
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165/177

&lt;222&gt; (13)...(333)

&lt;400&gt; 144

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	aac aaa gtg ctg agg tac aag ccc ccg ccg agc gaa tgt aac ccg gcc	96
	Asn Lys Val Leu Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala	
	15 20 25	
10	ttg gac gac ccg acg ccg gac tac atg aac ctg ctg ggc atg atc ttc	144
	Leu Asp Asp Pro Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe	
	30 35 40	
	agc atg tgc ggc ctc atg ctt aag ctg aag tgg tgt gct tgg gtc gct	192
	Ser Met Cys Gly Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala	
15	45 50 55 60	
	gtc tac tgc tcc ttc atc agc ttt gcc aac tct ccg agc tcg gag gac	240
	Val Tyr Cys Ser Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp	
	65 70 75	
	acg aag caa atg atg agt agc ttc atg ctg tcc atc tct gcc gtg gtg	288
20	Thr Lys Gln Met Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val	
	80 85 90	
	atg tcc tat ctg cag aat cct cag ccc atg acg ccc cca tgg	340
	Met Ser Tyr Leu Gln Asn Pro Gln Pro Met Thr Pro Pro Trp	
	95 100 105	
25	tgataccagc ctagaagggt cacattttgg acctgtcta tccactaggc ctgggctttg	390
	gctgctaaac ctgctgcctt cagctgccat cctggacttc cctgaatgag gccgtctcgg	450
	tgcctccagc tggatagagg gaacctggcc ctttcctagg gaacacctta ggcctaccoc	510
	tectgcctcc ctteccctgc ctgctgetgg gggagatget gtccatgttt ctagggggat	570
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&lt;210&gt; 145

&lt;211&gt; 864

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35 &lt;220&gt;

166/177

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&lt;222&gt; (111)...(785)

&lt;400&gt; 145

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	gagacgccgc ctccgatcc ccgcgcgggc gggaccgggc ggccggcacc atg acc	116
	Met Thr	
	1	
10	ctg ttt cac ttc ggg aac tgc ttc gct ctt gcc tac ttc ccc tac ttc	164
	Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro Tyr Phe	
	5 10 15	
	atc acc tac aag tgc agc ggc ctg tcc gag tac aac gcc ttc tgg aaa	212
	Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe Trp Lys	
	20 25 30	
15	tgc gtc cag gct gga gtc acc tac ctc ttt gtc caa ctc tgc aag atg	260
	Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys Lys Met	
	35 40 45 50	
	ctg ttc ttg gcc act ttc ttt ccc acc tgg gaa ggc ggc atc tat gac	308
	Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Gly Ile Tyr Asp	
20	55 60 65	
	ttc att ggg gag ttc atg aag gcc agc gtg gat gtg gca gac ctg ata	356
	Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp Leu Ile	
	70 75 80	
	ggc cta aac ctt gtc atg tcc cgg aat gcc ggc aag gga gag tac aag	404
25	Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu Tyr Lys	
	85 90 95	
	atc atg gtt gct gcc ctg ggc tgg gcc act gct gag ctt att atg tcc	452
	Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile Met Ser	
	100 105 110	
30	cgc tgc att ccc cta tgg gtc gga gcc cgg ggc att gag ttt gac tgg	500
	Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe Asp Trp	
	115 120 125 130	
	aag tac atc cag atg agc ata gac tcc aac atc agt ctg gtc cat tac	548
	Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val His Tyr	
35	135 140 145	

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 Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp Leu Tyr  
 150 155 160  
 cac acc ttc cgg cca gct gtc ctc ctg ctg atg ttc ctc agt gtc tac 644  
 5 His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser Val Tyr  
 165 170 175  
 aag gcc ttt gtt atg gag acc ttc gtc cac ctc tgc tcg ctg ggc agt 692  
 Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu Gly Ser  
 180 185 190  
 10 tgg gca gct cta ctg gcc cga gca gtg gta acg ggg ctg ctg gcc ctc 740  
 Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu Ala Leu  
 195 200 205 210  
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 Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser  
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 gtatttgaa agtt 864  
  
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 30 1 5  
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 Leu Val Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr  
 10 15 20 25  
 tac ctt ctg tcg gcc ctg ctc tct gct gcc ttc cta ctc gtg agg aaa 147  
 35 Tyr Leu Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys

168/177

			30				35				40																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																															</
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169/177

Asn Leu Asn Glu Leu Tyr Gln Arg Ala Lys Lys Leu Ser Lys Ala Gly  
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 Asp Asn Ile Pro Glu Glu Gln Pro Val Ala Ser Thr Pro Thr Thr Val  
 5 235 240 245  
 tca gat ggg gaa aac aag aag gat aaa taagatcctc ac 810  
 Ser Asp Gly Glu Asn Lys Lys Asp Lys  
 250 255  
 tttggcagtg ctccctctcc tgtcaattcc aggcctcttcc cataaccaca agcctgagge 870  
 10 tgcagccttt tatctatgtt ttccctttgg ctgtgactgg gtggggcagc atgcagcttc 930  
 tgattttaaa gaggcaccta gggaattgtc aggcacccca caggaaaggcc tgccatgctg 990  
 tggccaaactg ttctactgga gcaagaaaga gatctcatag gacggagggg gaaatggttt 1050  
 cctccaagc ttgggtcagt gtgttaactg cttatcagct attcagacat ctccatggtt 1110  
 tctccatgaa actctgtggt ttcatcattc cttcttagtt gacctgcaca gcttggttag 1170  
 15 acctagattt aaccctaagg taagatgctg ggtatagaa cgctaagaat tttcccccac 1230  
 ggactcttgc ttccttaagc cctcttggtt tegtcttagt tcttcattaa aagtataagc 1290  
 ctaactttgt cgctagtctt aaggagaaac ctttaaccac aaagtcttta tcattgaaga 1350  
 caatattgaa caaccccca tttgtgggg attgagaagg ggtgaataga ggcttgagac 1410  
 tttcctttgt gtggtaggac ttggaggaga aatcccttgg actttcacta accctctgac 1470  
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 gagcccgggc tgggtgcg atg gcc gcg gtg gtg gcc aag cgg gaa ggg ccg 170  
 Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro  
 35 1 5 10

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ccg ttc atc agc gag gcg gcc gtg cgg ggc aac gcc gcc gtc ctg gat      218
Pro Phe Ile Ser Glu Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp
          15          20          25
tat tgc cgg acc tcg gtg tca gcg ctg tcg ggg gcc acg gcc ggc atc      266
5 Tyr Cys Arg Thr Ser Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile
          30          35          40
ctc gcc ctc acc gcc ctc tac gcc ttc atc ttc tac ctg ctc gcc tcc      314
Leu Gly Leu Thr Gly Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser
          45          50          55
10 gtc ctg ctc tcc ctg ctc ctc att ctc aag gcg gga agg agg tgg aac      362
Val Leu Leu Ser Leu Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn
          60          65          70          75
aaa tat ttc aaa tca cgg aga cct ctc ttt aca gga gcc ctc atc ggg      410
Lys Tyr Phe Lys Ser Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly
15          80          85          90
ggc ctc ttc acc tac gtc ctg ttc tgg acg ttc ctc tac gcc atg gtg      458
Gly Leu Phe Thr Tyr Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val
          95          100          105
20 cac gtc tac tgaatgggg gcccgggga cttttttaa aaa      500
His Val Tyr
          110
ccagatcggg aggaactgtg ccagcaatta acaccatgta gaattcetta gttottaagt      560
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171/177

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cag tct cca tgg aga tta tct ttg ata aca gat ttc ttc tgg gga ata      157
5  Gln Ser Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile
    15           20           25           30
gct gag ttt gtg gtt ttg ttt ttc aaa act ctg ctt cag caa gat gtg      205
Ala Glu Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val
          35           40           45
10 aaa aaa aga aga agc tat gga aac tca tct gat tcc aga tat gat gat      253
Lys Lys Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp
          50           55           60
gga aga ggg cca cca gga aac cct ccc cga aga atg ggt aga atc aat      301
Gly Arg Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn
15 65           70           75
cat ctg cgt ggc cct agt ccc cct cca atg gct ggt gga tgaggaaggt      350
His Leu Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly
          80           85           90
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caagaagtgg aaggetgacc atgatgagca gtagatgaat gtgtatgtct aaacaaggac      470
tgctctgtgt cctcacagat gaatgaggtc atgctgggaa ttcctctctgc agggaaactgg      530
cctgactgac atgcagtccc ataaatgcag atgtttgtct cattaccttt ttgtatagtt      590
tattaaagta ttaatatagt ttaataaagt aaatatTTTT aggttgacaga atggactcct      650
catctttata ttcacgaaaa agcaactctga agaaaacaaa taaaagcctg tgtatttagc      710
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172/177

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	aag agc ctt ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc gcc ctc	151
5	Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu	
	20 25 30	
	ctc ctg cct cac tgc cag aag ctc ttt gtg tat gac ctt cac gca gtc	199
	Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val	
	35 40 45	
10	aag aac gac ttc cag att tgg agg ttg ata tgt gga aga ata att tgc	247
	Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys	
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	ctt gat ttg aaa gat act ttc tgc agt agt ctg ctt att tat aat ttt	295
	Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe	
15	65 70 75 80	
	agg ata ttt gaa aga aga tat gga agc aga aaa ttt gca tcc ttt ttg	343
	Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu	
	85 90 95	
	ctg ggt tcc tgg gtt ttg tca gcc tta ttt gac ttt ctc ctc att gaa	391
20	Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu	
	100 105 110	
	gct atg cag tat ttc ttt ggc atc act gca gct agt aat ttg cct tct	439
	Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser	
	115 120 125	
25	gga ttc ctg gca cct gcg ttt gct ctg ttt gta cca ttt tac tgc tcc	487
	Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser	
	130 135 140	
	ata cca aga gtc caa gtg gca caa att ctg ggt ccg ttg tcc atc aca	535
	Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr	
30	145 150 155 160	
	aac aag aca ttg att tat ata ttg gga ctg cag ctt ttc acc tct ggt	583
	Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly	
	165 170 175	
	tcc tac atc tgg att gta gcc ata agt gga ctt atg tcc ggt ctg tgc	631
35	Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys	

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	180	185	190	
	tac gac agc aaa atg ttc cag gtg cat cag gtg ctc tgc atc ccc agc			679
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser			
	195	200	205	
5	tgg atg gca aaa ttc ttt tct tgg aca ctt gaa ccc atc ttc tct tct			727
	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser			
	210	215	220	
	tca gaa ccc acc agc gaa gcc aga att ggg atg gga gcc acg ctg gac			775
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp			
10	225	230	235	240
	atc cag aga cag cag aga atg gag ctg ctg gac cgg cag ctg atg ttc			823
	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe			
	245	250	255	
	tct cag ttt gca caa ggg agg cga cag aga cag cag cag gga gga atg			871
15	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Gly Met			
	260	265	270	
	atc aat tgg aat cgt ctt ttt cct cct tta cgt cag cga caa aac gta			919
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val			
	275	280	285	
20	aac tat cag ggc ggt cgg cag tct gag cca gca gcg ccc cct cta gaa			967
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu			
	290	295	300	
	gct tct gag gaa cag gtc gcc cgg ctc atg gag atg gga ttt tcc aga			1015
	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg			
25	305	310	315	320
	ggc gat gct ttg gaa gcc ctg aga gct tca aac aat gac ctc aat gtc			1063
	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val			
	325	330	335	
	gcc acc aac ttc ctg ctg cag cac tgatagtcac aggcacacac tgg			1110
30	Ala Thr Asn Phe Leu Leu Gln His			
	340			
	gaccggaccg gcagccgagt gacagtgcgt ggtccccacc atcagatcag cccggggacc			1170
	gagcatctct ggtgctgatg ttcttggtggg aagagggagg ttccaccgca cccctgcct			1230
	caaccgcaag actgttgccg ttttagtggt gagataagtt tgccattaca ttagcatgta			1290
35	ttttctatct atatttttta ttgggcattt tccctaggtt ggagagtcag cactcgtttt			1350

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 cctggcgccg acctgctcaa gaccagggtc ctgccaagcg ctaggagggc gcgtgccagg 180  
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 Met Gly Pro Pro Pro Gly Ala  
 30 1 5  
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 Gly Val Ser Cys Arg Gly Gly Cys Gly Phe Ser Arg Leu Leu Ala Trp  
 10 15 20  
 tgc ttc ctg ctg gcc ctg agt ccg cag gca ccc ggt tcc cgg ggg gct 327  
 35 Cys Phe Leu Leu Ala Leu Ser Pro Gln Ala Pro Gly Ser Arg Gly Ala

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	25	30	35	
	gaa gca gtg tgg acc gcg tac ctc aac gtg tcc tgg cgg gtt ccg cac			375
	Glu Ala Val Trp Thr Ala Tyr Leu Asn Val Ser Trp Arg Val Pro His			
	40	45	50	55
5	acg gga gtg aac cgt acg gtg tgg gag ctg agc gag gag ggc gtg tac			423
	Thr Gly Val Asn Arg Thr Val Trp Glu Leu Ser Glu Glu Gly Val Tyr			
	60	65	70	
	ggc cag gac tgg ccg ctg gag cct gtg gct ggg gtc ctg gta ccg ccc			471
	Gly Gln Asp Ser Pro Leu Glu Pro Val Ala Gly Val Leu Val Pro Pro			
10	75	80	85	
	gac ggg ccc ggg gcg ctt aac gcc tgt aac ccg cac acg aat ttc acg			519
	Asp Gly Pro Gly Ala Leu Asn Ala Cys Asn Pro His Thr Asn Phe Thr			
	90	95	100	
	gtg ccc acg gtt tgg gga agc acc gtg caa gtc tct tgg ttg gcc ctc			567
15	Val Pro Thr Val Trp Gly Ser Thr Val Gln Val Ser Trp Leu Ala Leu			
	105	110	115	
	atc caa cgc gcc ggg gcc tgc acc ttc gca gac aag atc cat ctg gct			615
	Ile Gln Arg Gly Gly Gly Cys Thr Phe Ala Asp Lys Ile His Leu Ala			
	120	125	130	135
20	tat gag aga ggg gcg tct gga gcc gtc atc ttt aac ttc ccc ggg acc			663
	Tyr Glu Arg Gly Ala Ser Gly Ala Val Ile Phe Asn Phe Pro Gly Thr			
	140	145	150	
	cgc aat gag gtc atc ccc atg tct cac ccg ggt gca gta gac att gtt			711
	Arg Asn Glu Val Ile Pro Met Ser His Pro Gly Ala Val Asp Ile Val			
25	155	160	165	
	gca atc atg atc gcc aat ctg aaa gcc aca aaa att ctg caa tct att			759
	Ala Ile Met Ile Gly Asn Leu Lys Gly Thr Lys Ile Leu Gln Ser Ile			
	170	175	180	
	caa aga gcc ata caa gtg aca atg gtc ata gaa gta ggg aaa aaa cat			807
30	Gln Arg Gly Ile Gln Val Thr Met Val Ile Glu Val Gly Lys Lys His			
	185	190	195	
	ggc cct tgg gtg aat cac tat tca att ttt ttc gtt tct gtg tcc ttt			855
	Gly Pro Trp Val Asn His Tyr Ser Ile Phe Phe Val Ser Val Ser Phe			
	200	205	210	215
35	ttt att att acg gcg gca act gtg gcc tat ttt atc ttt tat tct gct			903

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	Phe Ile Ile Thr Ala Ala Thr Val Gly Tyr Phe Ile Phe Tyr Ser Ala	
	220 225 230	
	cga agg cta cgg aat gca aga gct caa agc agg aag cag agg caa tta	951
	Arg Arg Leu Arg Asn Ala Arg Ala Gln Ser Arg Lys Gln Arg Gln Leu	
5	235 240 245	
	aag gca gat gct aaa aaa gct att gga agg ctt caa cta cgc aca ctg	999
	Lys Ala Asp Ala Lys Lys Ala Ile Gly Arg Leu Gln Leu Arg Thr Leu	
	250 255 260	
	aaa caa gga gac aag gaa att ggc cct gat gga gat agt tgt gct gtg	1047
10	Lys Gln Gly Asp Lys Glu Ile Gly Pro Asp Gly Asp Ser Cys Ala Val	
	265 270 275	
	tgc att gaa ttg tat aaa cca aat gat ttg gta cgc atc tta acg tgc	1095
	Cys Ile Glu Leu Tyr Lys Pro Asn Asp Leu Val Arg Ile Leu Thr Cys	
	280 285 290 295	
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	Asn His Ile Phe His Lys Thr Cys Val Asp Pro Trp Leu Leu Glu His	
	300 305 310	
	agg act tgc ccc atg tgc aaa tgt gac ata ctc aaa gct ttg gga att	1191
	Arg Thr Cys Pro Met Cys Lys Cys Asp Ile Leu Lys Ala Leu Gly Ile	
20	315 320 325	
	gag gtg gat gtt gaa gat gga tca gtg tct tta caa gtc cct gta tcc	1239
	Glu Val Asp Val Glu Asp Gly Ser Val Ser Leu Gln Val Pro Val Ser	
	330 335 340	
	aat gaa ata tct aat agt gcc tcc tcc cat gaa gag gat aat cgc agc	1287
25	Asn Glu Ile Ser Asn Ser Ala Ser Ser His Glu Glu Asp Asn Arg Ser	
	345 350 355	
	gag acc gca tca tct gga tat gct tca gta cag gga aca gat gaa ccc	1335
	Glu Thr Ala Ser Ser Gly Tyr Ala Ser Val Gln Gly Thr Asp Glu Pro	
	360 365 370 375	
30	cct ctg gag gaa cac gtg cag tca aca aat gaa agt cta cag ctg gta	1383
	Pro Leu Glu Glu His Val Gln Ser Thr Asn Glu Ser Leu Gln Leu Val	
	380 385 390	
	aac cat gaa gca aat tct gtg gca gtg gat gtt att cct cat gtt gac	1431
	Asn His Glu Ala Asn Ser Val Ala Val Asp Val Ile Pro His Val Asp	
35	395 400 405	



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5  Arg Glu Ile Lys Ser
      425
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